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=> fil reg
FILE 'REGISTRY' ENTERED AT 17:13:39 ON 21 JAN 2003
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provided by InfoChem.

STRUCTURE FILE UPDATES:   20 JAN 2003  HIGHEST RN 479577-81-6
DICTIONARY FILE UPDATES:  20 JAN 2003  HIGHEST RN 479577-81-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d sta que l17
L14                 STR
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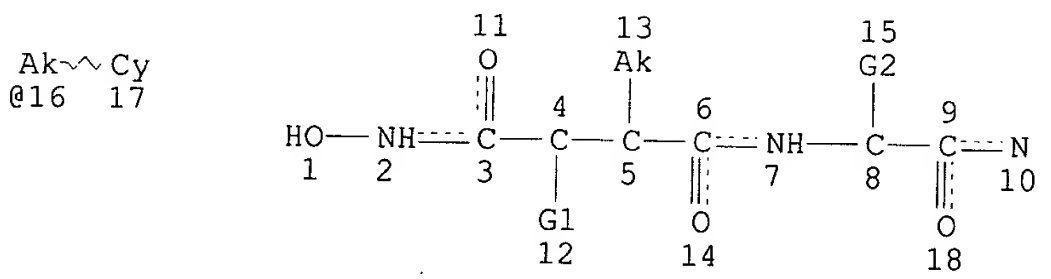


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VAR G2=AK/16
NODE ATTRIBUTES:
CONNECT IS M1  RC AT  10
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  18

STEREO ATTRIBUTES: NONE
L16         2264 SEA FILE=REGISTRY SSS FUL L14
L17          629 SEA FILE=REGISTRY SUB=L16 CSS FUL L14

100.0% PROCESSED   2264 ITERATIONS                    629 ANSWERS
SEARCH TIME: 00.00.01


=> d his

     (FILE 'HOME' ENTERED AT 15:52:25 ON 21 JAN 2003)
                SET COST OFF

     FILE 'REGISTRY' ENTERED AT 15:52:46 ON 21 JAN 2003
L1             2 S HYALURONIC ACID/CN OR 9067-32-7
L2           753 S ?HYALURON?/CNS NOT L1
```

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

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L3          435 S L2 NOT SQL/FA
L4          318 S L2 NOT L3
                E CYCLOOXYGENASE/CN
L5            1 S E8
L6            2 S E3,E7
                E MATRIX METALLOPROTEASE/CN
L7           15 S E3,E5-E13,E15-E17,E23,E24
L8            5 S E25,E36,E43,E45,E46
L9            4 S E50,E51,E55,E58
L10           1 S E61
L11           5 S E72,E75,E79-E81
L12           4 S E85,E89-E91
L13        1365 S (?METALLOPROTEINASE? OR ?METALLOPROTEASE?)/CNS
L14             STR
L15          31 S L14 CSS
L16        2264 S L14 FUL
                SAV TEMP L16 FONDA700/A
L17         629 S L14 CSS FUL SUB=L16
                SAV L17 FONDA700A/A

     FILE 'HCAPLUS' ENTERED AT 16:16:23 ON 21 JAN 2003
L18       10031 S L1
L19        3440 S L3
L20         151 S L4
L21       14614 S HYALURONIC ACID OR HYALURONATE OR HYALURONAN
L22       20161 S ?HYALURON?
L23       20696 S L18-L22
L24        1922 S L5
L25        9113 S L6
L26       13384 S (COX OR CYCLOOXYGENASE OR CYCLO OXYGENASE)(L)2 OR COX2
L27          13 S PROSTAGLANDIN(L)(ENDOPEROXIDASE OR ENDO PEROXIDASE)(L)(SYNTHA
L28          41 S L23 AND L24-L27
L29       26594 S L7-L13
L30         476 S L23 AND L29
L31         309 S L17
L32           4 S L23 AND L31

     FILE 'REGISTRY' ENTERED AT 16:21:16 ON 21 JAN 2003
L33        1635 S L16 NOT L17

     FILE 'HCAPLUS' ENTERED AT 16:21:22 ON 21 JAN 2003
L34           3 S L33 AND L23
L35          45 S L28,L32,L34
                E ANTIRHEUMAT/CT
                E E5+ALL
L36        4437 S E5,E4+NT
L37          48 S L23 AND L36
L38          91 S L35,L37
L39          77 S L23 AND (ANTIRHEUMAT? OR ANTI RHEUMAT?)
L40         136 S L38,L39
L41           6 S L40 AND ?CONJUGAT?
                E TAMURA T/AU
L42         596 S E3-E5
                E TAMURA TATSUYA/AU
L43          57 S E3
                E OKAMACHI A/AU
L44          15 S E3,E4
                E CHUGAI/PA,CS
L45        3920 S E1-E4
                E SEIYAKU/PA,CS
L46       15106 S E1-E6
                E KABUSHIKI/PA,CS
L47           1 S E10E4
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                E KAISHA/PA,CS
L48         14062 S E2-E4
                E KABUSHIKI/PA,CS
L49          8315 S E1-E4
L50             3 S L40 AND L42-L49
                E WO99-JP2600/AP,PRN
L51             1 S E3,E4
                E JP98-138329/AP,PRN
L52             1 S E4
                E JP98-224187/AP,PRN
L53             1 S E4
                E JP99-43064/AP,PRN
L54             1 S E4
L55             0 S L40 AND L51-L54
L56             1 S L51-L54 AND L42-L49

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L57             1 S 9001-92-7

     FILE 'HCAPLUS' ENTERED AT 16:29:06 ON 21 JAN 2003
L58         34671 S L57
L59        135094 S ?PROTEASE? OR ?PROTEINASE?
L60           972 S L23 AND L58,L59
L61             8 S L60 AND L42-L49
                  SEL DN AN 1-3
L62             3 S L61 AND E1-E9
L63             4 S L50,L56,L62 AND L18-L32,L34-L56,L58-L62
L64           117 S L23 AND L59 (L) ?MATRIX? (L) ?METALLO?
L65           246 S L40,L64
L66             4 S L56,L63
                E JOINT/CT
                E E5+ALL
L67          1229 S E2
                E JOINT/CT
L68          3685 S E7-E28
                E E6+ALL
L69          8769 S E6,E5+NT
                E E13+ALL
L70          2565 S E2
L71            25 S L65 AND L67-L70
                E CARTILAGE/CT
L72            13 S L65 AND E4-E20
                E E3+ALL
L73            38 S L65 AND E7+NT
                E RHEUMATISM/CT
                E E3+ALL
                E E2+ALL
L74            48 S L65 AND E4,E5,E3+NT
L75            77 S L71-L74
L76           170 S L40,L75
L77          3545 S (L1 OR L3 OR L4)(L)(THU OR USES OR BUU OR BAC OR DMA OR PAC O
L78            45 S L76 AND L77
L79            43 S L78 NOT L66
L80            79 S L76 AND (1 OR 63)/SC,SX
L81            76 S L80 NOT L66
L82            84 S L79,L81
L83            53 S L82 AND (?CONJUGAT? OR SYNERG? OR BIND? OR BOUND? OR REACT? O
L84            19 S L83 AND L29
L85            21 S L83 AND L58,L59
                  SEL DN AN 8 18
L86             2 S E1-E6
L87            27 S L83 NOT L84,L85,L86,L66
                  SEL DN AN 8 15 18
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L88           3 S E7-E15
L89          31 S L82 NOT L83-L88
                SEL DN AN 11 12
L90           2 S E16-E21
L91          11 S L66,L86,L88,L90
L92       12795 S L18-L20
L93          25 S L92 AND L24,L25
L94         580 S L92 AND L29,L58
L95           3 S L92 AND L31
L96           3 S L92 AND L33
L97           3 S L95,L96
L98           1 S L97 AND L91
L99          11 S L91,L98
L100         35 S L94 AND L36,L67-70
L101         40 S L94 AND L76
L102         59 S L100,L101
L103         31 S L102 NOT L82-L91,L99
                SEL DN AN 12
L104          1 S L103 AND E22-E24
L105         12 S L99,L104 AND L18-L32,L34-L56,L58-104
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 17:11:11 ON 21 JAN 2003
L106         19 S E25-E43

     FILE 'HCAPLUS' ENTERED AT 17:11:28 ON 21 JAN 2003
                SEL RN L66

     FILE 'REGISTRY' ENTERED AT 17:12:01 ON 21 JAN 2003
L107         36 S E44-E79
L108         23 S L107 NOT L106
L109          1 S L108 AND C39H59N5O11

     FILE 'HCAPLUS' ENTERED AT 17:13:17 ON 21 JAN 2003
L110          1 S L109
L111         12 S L110,L105

     FILE 'REGISTRY' ENTERED AT 17:13:39 ON 21 JAN 2003

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 17:13:54 ON 21 JAN 2003
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FILE COVERS 1907 - 21 Jan 2003 VOL 138 ISS 4
FILE LAST UPDATED: 20 Jan 2003 (20030120/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l111 all hitstr tot

L111 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:504633 HCAPLUS
DN 137:52423
TI Drugs against articular failure containing amino sugars and trehalose
IN Fukuda, Shigeharu; Ario, Takeshi; Miyake, Toshio
PA **Kabushiki Kaisha** Hayashibara Seibutsu Kagaku Kenkyujo, Japan
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM A61K031-7008
ICS A61K031-727; A61K031-728; A61K031-7016; A61P019-02; A61P029-00; A61K031-7008; A61K031-7016; A61K031-726; A61K031-7016; A61K031-727; A61K031-7016; A61K031-728; A61K031-7016
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): **1**, 18, 62
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002051424	A1	20020704	WO 2001-JP11147	20011219
	WO 2002051424	C1	20020801		
	W: KR, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	JP 2002193811	A2	20020710	JP 2000-391390	20001222
PRAI	JP 2000-391390	A	20001222		

AB It is intended to provide compns. which exert an effect of restoring articular failure at a level superior to aminosugars and glycosaminoglycan. This problem is solved by providing drugs against articular failure which contain as the active ingredients an aminosugar and trehalose. The compns. contg. aminosugar and trehalose are suitable for use in oral pharmaceutical compns., cosmetics, and foods. A powder compn. contg. trehalose (Treha) 4, glucosamine 1 parts was prepd. for use in a pharmaceutical, cosmetic, or food compn.
ST aminosugar trehalose articular disorder treatment
IT Carbohydrates, biological studies
RL: COS (Cosmetic use); FFD (Food or feed use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino sugars; compns. contg. amino sugars and trehalose for treatment of articular disorder)
IT Antiarthritics
Antirheumatic agents
Arthritis
Bath preparations
Chewing gum
Cosmetics
Food
Rheumatic diseases
(compns. contg. amino sugars and trehalose for treatment of articular disorder)
IT Glycosaminoglycans, biological studies
RL: COS (Cosmetic use); FFD (Food or feed use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. amino sugars, trehalose, and glycosaminoglycans for treatment of articular disorder)
IT **Joint, anatomical**
(**disease**; compns. contg. amino sugars and trehalose for treatment of articular disorder)
IT Beverages
(health; compns. contg. amino sugars and trehalose for treatment of

articular disorder)
IT Drug delivery systems
(oral; compns. contg. amino sugars and trehalose for treatment of articular disorder)
IT 99-20-7, Trehalose 3416-24-8, Glucosamine 7512-17-6, N-Acetyl glucosamine 14307-02-9, Mannosamine
RL: COS (Cosmetic use); FFD (Food or feed use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. amino sugars and trehalose for treatment of articular disorder)
IT **9004-61-9, Hyaluronic acid** 9005-49-6, Heparin, biological studies 9007-27-6, Chondroitin 9007-28-7, Chondroitin sulfate 9050-30-0, Heparan sulfate 9056-36-4, Keratan sulfate 24967-93-9, Chondroitin 4-sulfate 24967-94-0, Dermatan sulfate
RL: COS (Cosmetic use); FFD (Food or feed use); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(compns. contg. amino sugars, trehalose, and glycosaminoglycans for treatment of articular disorder)
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) K K Hayashibara Seibutsu Kagaku Kenkyujo; JP 2000198736 A 2000 HCAPLUS
(2) Nutramax Lab Inc; EP 0693928 A 1994 HCAPLUS
(3) Nutramax Lab Inc; JP 09503197 A 1994
(4) Nutramax Lab Inc; ES 2099686 T 1994
(5) Nutramax Lab Inc; CA 2159591 A 1994 HCAPLUS
(6) Nutramax Lab Inc; NZ 263710 A 1994
(7) Nutramax Lab Inc; AU 6490194 A 1994
(8) Nutramax Lab Inc; AU 688313 A 1994 HCAPLUS
(9) Nutramax Lab Inc; DE 693928 T 1994
(10) Nutramax Lab Inc; BR 9406178 A 1994 HCAPLUS
(11) Nutramax Lab Inc; WO 9422453 A 1994 HCAPLUS
(12) Nutramax Lab Inc; FI 954654 A 1994
(13) Sunstar Inc; JP 200172582 A 2001
(14) Takeda Chemical Industries Ltd; JP 2001302496 A 2001 HCAPLUS
IT **9004-61-9, Hyaluronic acid**
RL: COS (Cosmetic use); FFD (Food or feed use); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(compns. contg. amino sugars, trehalose, and glycosaminoglycans for treatment of articular disorder)
RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

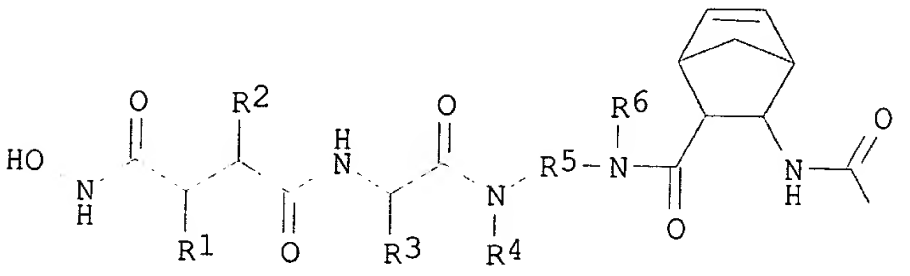
L111 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:428944** HCAPLUS
DN **137:24315**
TI Compound of hydroxamic acid derivative and **hyaluronic acid** for treatment of joint disease
IN Ikeya, Hitoshi; Morikawa, Tadashi; Takahashi, Koichi; **Okamachi, Akira**; **Tamura, Tatsuya**
PA **Chugai Seiyaku Kabushiki Kaisha**, Japan; Denki Kagaku Kogyo **Kabushiki Kaisha**
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C08B037-08
ICS A61K031-728; A61P019-02; A61P029-00
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): **1**

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002044218	A1	20020606	WO 2001-JP10493	20011130
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002018512	A5	20020611	AU 2002-18512	20011130
PRAI	JP 2000-363993	A	20001130		
	WO 2001-JP10493	W	20011130		

OS MARPAT 137:24315

GI



I

AB Disclosed is a compd. having MMP inhibitory activity which is a compd. of a hydroxamic acid deriv. I and **hyaluronic acid**, wherein R1 = H, OH, C1-8 alkyl, etc.; R2 = C1-8 alkyl, etc.; R3 = C1-8 alkyl, etc.; R4 = H, C1-4 alkyl; R5 = -R7-R8-R9- (R7 = C1-8 alkylene, R8 = methylene, imino, O, etc., and R9 = C1-10 alkylene, etc.); and R6 = H, C1-4 alkyl, provided that R1 and R3 in combination may form a ring. The compd. comprises a group I and any of **hyaluronic acid**, a deriv. thereof, and salts of these, the former being bonded to a hydroxyl group of the latter through a carbamate linkage. Sodium **hyaluronate** was reacted with N-hydroxy-5-norbornene-2,3-dicarboxyimide (HONB) and hydroxamic acid deriv. N'-(13-amino-4,7,10-trioxatridecanyl)-N-(3S-hydroxy-4-(N-(1-methoxy-1-methylethoxy)amino)-2R-isobutylsuccinyl)-L-tert-leucinamide. The obtained compd. showed excellent inhibitory effect on gelatinase A and stromelysin-1 in in vitro test.

ST **hyaluronate** hydroxamate deriv prepn **matrix metalloproteinase** inhibitor

IT **Joint, anatomical**
(**disease; hyaluronic acid** hydroxamate derivs. for treatment of joint **disease**)

IT Antiarthritics
Antirheumatic agents
(**hyaluronic acid** hydroxamate derivs. for treatment of joint disease)

IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**hyaluronic acid** hydroxamate derivs. for treatment of joint disease)

IT **434283-17-7DP**, compexes with **hyaluronic acid**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**hyaluronic acid** hydroxamate derivs. for treatment of joint disease)

IT **434283-18-8D**, reaction products with **hyaluronate** derivs.
434283-19-9D, reaction products with **hyaluronate** derivs.
434283-20-2D, reaction products with **hyaluronate** derivs.
434283-21-3D, reaction products with **hyaluronate** derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hyaluronic acid** hydroxamate derivs. for treatment of joint disease)

IT **79955-99-0**, Stromelysin-1 **141907-41-7**, **Matrix metalloproteinase 146480-35-5**, Gelatinase A
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of; **hyaluronic acid** hydroxamate derivs. for treatment of joint disease)

IT 116-11-0 5470-11-1, Hydroxyammonium chloride **9067-32-7**, Sodium **hyaluronate** 21715-90-2, HONb 62965-35-9, N-(tert-Butoxycarbonyl)-L-tert-leucine 157518-70-2 220156-99-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of **hyaluronic acid** hydroxamate derivs. for treatment of joint disease)

IT 433708-29-3P 433708-31-7P 433708-33-9P 433708-35-1P
433708-37-3P 433708-39-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of **hyaluronic acid** hydroxamate derivs. for treatment of joint disease)

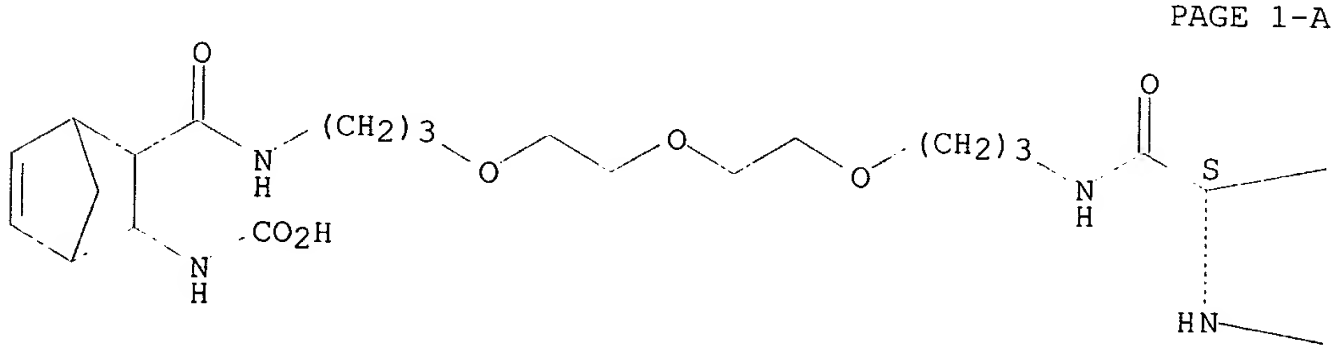
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Chugai Pharmaceutical Co Ltd; EP 1082963 A 1999 HCAPLUS
(2) Chugai Pharmaceutical Co Ltd; WO 9959603 A 1999 HCAPLUS
(3) Shionogi & Co Ltd; WO 0046189 A 2000 HCAPLUS

IT **434283-17-7DP**, compexes with **hyaluronic acid**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**hyaluronic acid** hydroxamate derivs. for treatment of joint disease)

RN 434283-17-7 HCAPLUS
CN Carbamic acid, [3-[(18S,21R)-18-(1,1-dimethylethyl)-21-[(1S)-1-hydroxy-2-(hydroxyamino)-2-oxoethyl]-23-methyl-1,17,20-trioxo-6,9,12-trioxa-2,16,19-triazatetracos-1-yl]bicyclo[2.2.1]hept-5-en-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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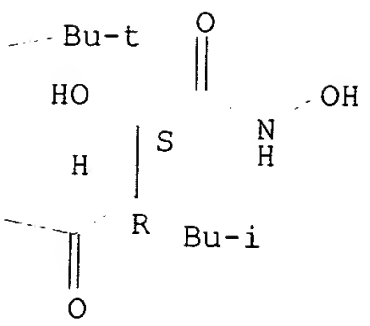


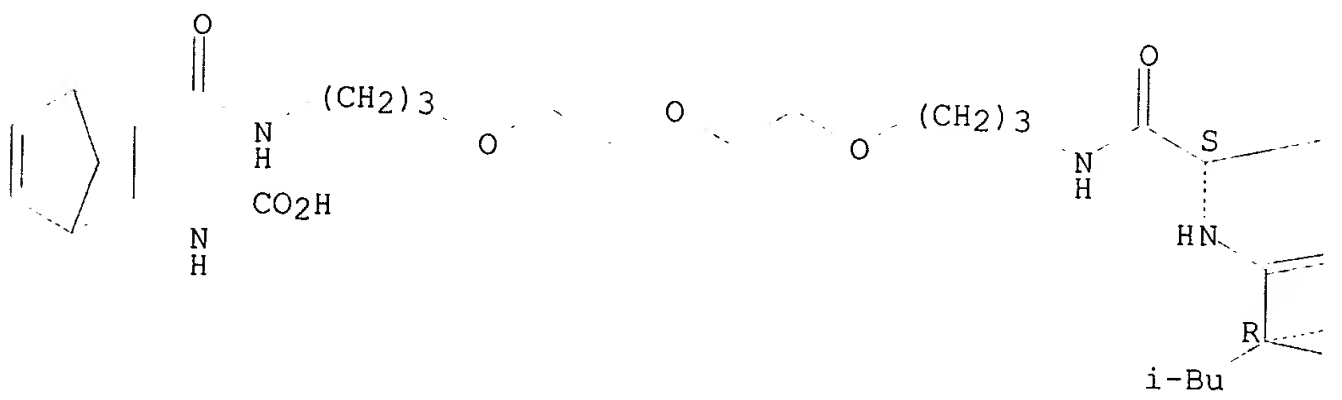
IT **434283-18-8D**, reaction products with **hyaluronate** derivs.
434283-19-9D, reaction products with **hyaluronate** derivs.
434283-20-2D, reaction products with **hyaluronate** derivs.
434283-21-3D, reaction products with **hyaluronate** derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hyaluronic acid** hydroxamate derivs. for treatment of joint disease)

RN 434283-18-8 HCAPLUS

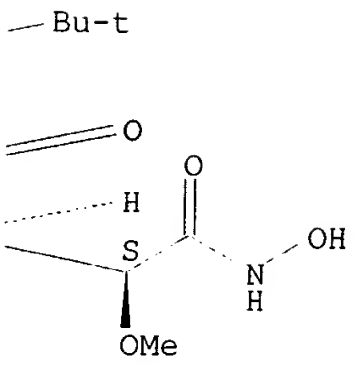
CN Carbamic acid, [3-[(18S,21R,22S)-18-(1,1-dimethylethyl)-22-[(hydroxyamino)carbonyl]-21-(2-methylpropyl)-1,17,20-trioxo-6,9,12,23-tetraoxa-2,16,19-triazatetracos-1-yl]bicyclo[2.2.1]hept-5-en-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



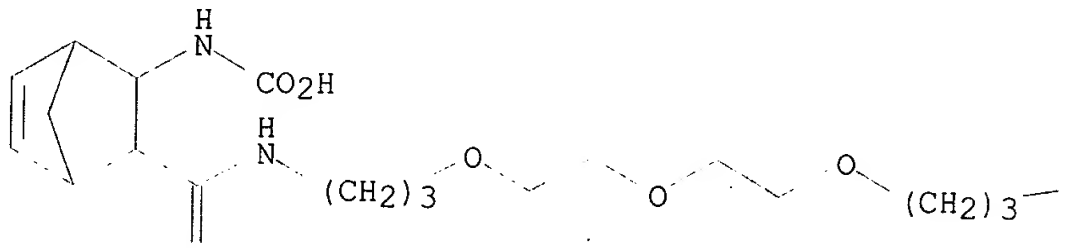
PAGE 1-B



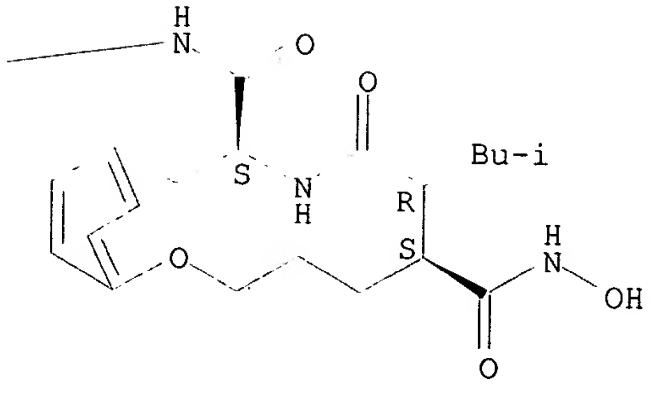
RN 434283-19-9 HCAPLUS
CN Carbamic acid, [3-[17-[(6S,7R,10S)-6-[(hydroxyamino)carbonyl]-7-(2-methylpropyl)-8-oxo-2-oxa-9-azabicyclo[10.2.2]hexadeca-12,14,15-trien-10-yl]-1,17-dioxo-6,9,12-trioxa-2,16-diazaheptadec-1-yl]bicyclo[2.2.1]hept-5-en-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



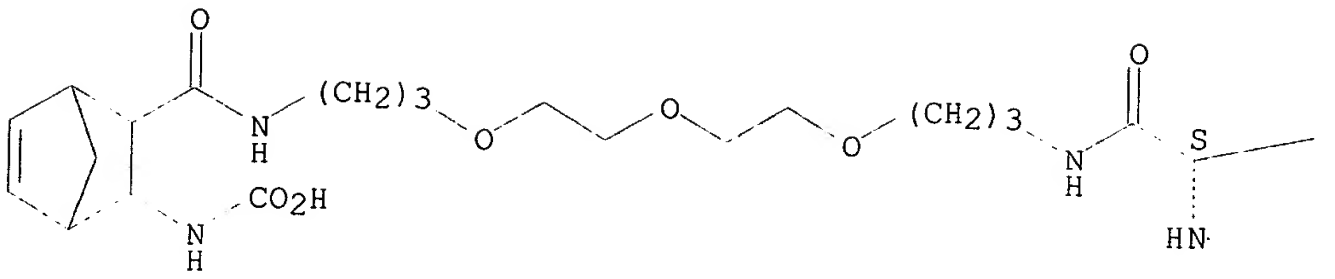
PAGE 1-B



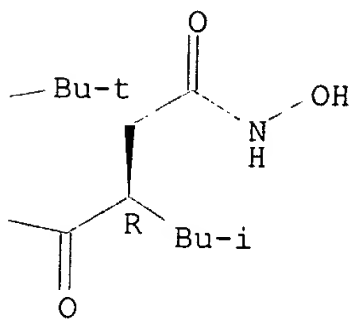
RN 434283-20-2 HCAPLUS
CN Carbamic acid, [3-[(18S,21R)-18-(1,1-dimethylethyl)-21-[2-(hydroxyamino)-2-oxoethyl]-23-methyl-1,17,20-trioxo-6,9,12-trioxa-2,16,19-triazatetracos-1-yl]bicyclo[2.2.1]hept-5-en-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



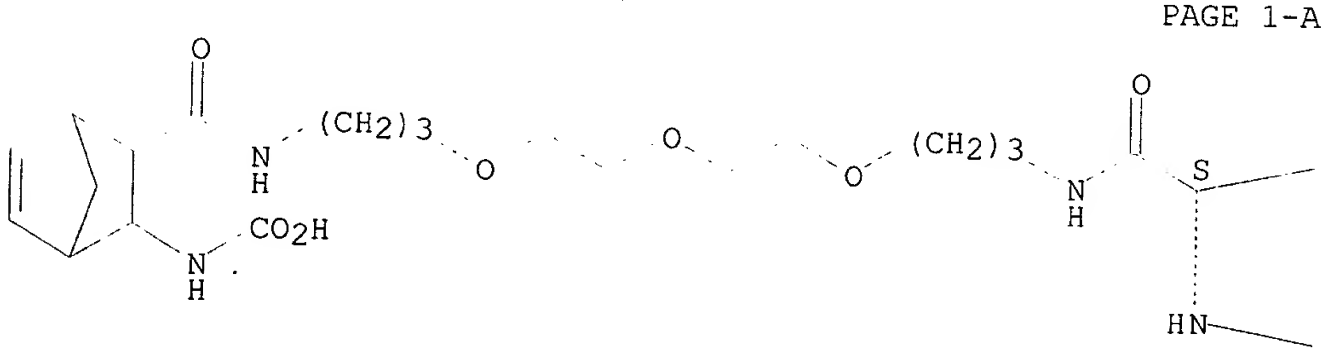
PAGE 1-B



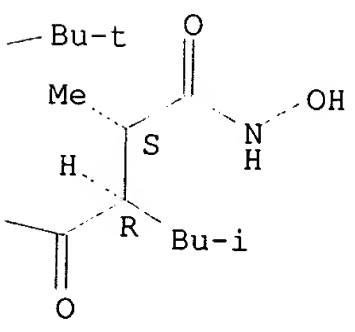
RN 434283-21-3 HCAPLUS
CN Carbamic acid, [3-[(18S,21R)-18-(1,1-dimethylethyl)-21-[(1S)-2-(hydroxyamino)-1-methyl-2-oxoethyl]-23-methyl-1,17,20-trioxo-6,9,12-trioxa-2,16,19-triazatetracos-1-yl]bicyclo[2.2.1]hept-5-en-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT **79955-99-0**, Stromelysin-1 **141907-41-7**, **Matrix**

metalloproteinase 146480-35-5, Gelatinase A
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of; **hyaluronic acid** hydroxamate derivs.
for treatment of joint disease)
RN 79955-99-0 HCAPLUS
CN Stromelysin 1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 141907-41-7 HCAPLUS
CN Proteinase, matrix metallo- (9CI) (CA INDEX NAME)

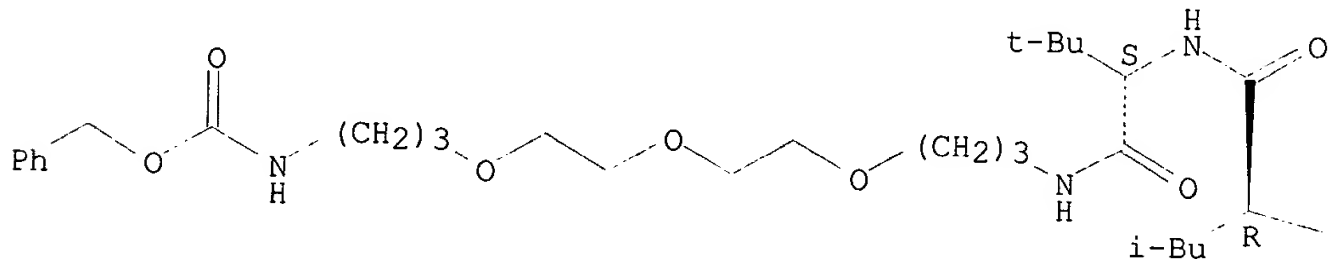
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 146480-35-5 HCAPLUS
CN Gelatinase A (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9067-32-7**, Sodium **hyaluronate**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of **hyaluronic acid** hydroxamate derivs. for
treatment of joint disease)
RN 9067-32-7 HCAPLUS
CN Hyaluronic acid, sodium salt (9CI) (CA INDEX NAME)

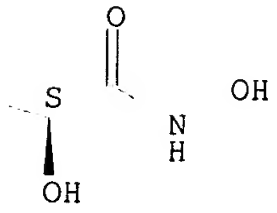
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **433708-37-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of **hyaluronic acid** hydroxamate derivs. for
treatment of joint disease)
RN 433708-37-3 HCAPLUS
CN 6,9,12-Trioxa-2,16,19-triazatetracosanoic acid, 18-(1,1-dimethylethyl)-21-[(1S)-1-hydroxy-2-(hydroxyamino)-2-oxoethyl]-23-methyl-17,20-dioxo-, phenylmethyl ester, (18S,21R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L111 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2003 ACS

AN **2000:880946** HCAPLUS
DN **134:25362**
TI Use of catechins for arthritis treatment, **compositions**, and screening method
IN Buttle, David; Adcocks, Clair; Collin, Peter
PA University of Sheffield, UK
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 1-7 (Pharmacology)
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000074662	A2	20001214	WO 2000-GB2048	20000606
	WO 2000074662	A3	20020314		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1207862	A2	20020529	EP 2000-935346	20000606
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003501381	T2	20030114	JP 2001-501199	20000606
PRAI	US 1999-137699P	P	19990607		
	GB 2000-7321	A	20000327		
	WO 2000-GB2048	W	20000606		

AB The invention relates to the use of catechins in the treatment of various forms of arthritis, including the use of **combinations** of catechins and other anti-arthritic agents in the treatment; medicaments and **compns**. for use in the treatment; and methods to identify agents with anti-arthritic properties.

ST screening arthritis inhibitor catechin

IT Blood cell
(TNF-.alpha. synthesis in; catechins for arthritis treatment, **compns**., and screening method)

IT **Arthritis**
(acute pyrophosphate; catechins for arthritis treatment, **compns**., and screening method)

IT Flavanols
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and catechin-**hyaluronic acid conjugates**; catechins for arthritis treatment, **compns**., and screening method)

IT Spinal column
(ankylosing spondylitis; catechins for arthritis treatment, **compns**., and screening method)

IT **Joint, anatomical**
(**bursa**, bursitis; catechins for arthritis treatment, **compns**., and screening method)

IT Musculoskeletal diseases
(cartilage, chondrolysis; catechins for arthritis treatment, **compns**., and screening method)

IT Antiarthritics
Antirheumatic agents

Cartilage
Drug screening
Gout
Lupus erythematosus
Sjogren's syndrome
(catechins for arthritis treatment, **compns**., and screening method)

IT Biopolymers
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(catechins for arthritis treatment, **compns**., and screening method)

IT Proteoglycans, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(catechins for arthritis treatment, **compns**., and screening method)

IT Interleukin 1.alpha.
Interleukin 1.beta.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(catechins for arthritis treatment, **compns**., and screening method)

IT **Cartilage**
(**disease**, chondrolysis; catechins for arthritis treatment, **compns**., and screening method)

IT Immune system
(immune-silent **compn**.; catechins for arthritis treatment, **compns**., and screening method)

IT **Chondrocyte**
(lactate output; catechins for arthritis treatment, **compns**., and screening method)

IT **Bone, disease**
Cartilage
(**osteochondritis**, and relapsing polychondritis; catechins for arthritis treatment, **compns**., and screening method)

IT Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pro-inflammatory; catechins for arthritis treatment, **compns**., and screening method)

IT **Arthritis**
(pseudogout; catechins for arthritis treatment, **compns**., and screening method)

IT **Arthritis**
(**reactive**, and psoriatic and juvenile; catechins for arthritis treatment, **compns**., and screening method)

IT Glycosaminoglycans, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(sulfated; catechins for arthritis treatment, **compns**., and screening method)

IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type II; catechins for arthritis treatment, **compns**., and screening method)

IT Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(.alpha.; catechins for arthritis treatment, **compns**., and screening method)

IT 154-23-4, (+)-Catechin 154-23-4D, (+)-Catechin, **hyaluronic acid conjugates** 490-46-0, (-)-Epicatechin 490-46-0D,

(-)-Epicatechin, **hyaluronic acid conjugates**
970-74-1, (-)-Epigallocatechin 970-74-1D, (-)-Epigallocatechin, **hyaluronic acid conjugates** 989-51-5, (-)-Epigallocatechin gallate 989-51-5D, (-)-Epigallocatechin gallate, **hyaluronic acid conjugates** 1257-08-5
1257-08-5D, **hyaluronic acid conjugates**
3371-27-5, (-)-Gallocatechin 3371-27-5D, (-)-Gallocatechin, **hyaluronic acid conjugates** 3416-24-8, Glucosamine 4233-96-9, (-)-Gallocatechin gallate 4233-96-9D, (-)-Gallocatechin gallate, **hyaluronic acid conjugates 9004-61-9, Hyaluronic acid 9004-61-9D, Hyaluronic acid, conjugates** with catechins 18829-70-4, (-)-Catechin
18829-70-4D, (-)-Catechin, **hyaluronic acid conjugates** 29031-19-4, Glucosamine sulfate 35323-91-2, (+)-Epicatechin 35323-91-2D, (+)-Epicatechin, **hyaluronic acid conjugates** 130405-40-2, (-)-Catechin gallate
130405-40-2D, (-)-Catechin gallate, **hyaluronic acid conjugates**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(catechins for arthritis treatment, **compns.**, and screening method)

IT 302-79-4, all-trans-Retinoic acid 11103-57-4D, Vitamin A, metabolites
106956-32-5, Oncostatin M
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(catechins for arthritis treatment, **compns.**, and screening method)

IT 50-21-5, Lactic acid, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chondrocyte lactate output; catechins for arthritis treatment, **compns.**, and screening method)

IT **9004-61-9, Hyaluronic acid 9004-61-9D, Hyaluronic acid, conjugates** with catechins
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(catechins for arthritis treatment, **compns.**, and screening method)

RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L111 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:645863** HCAPLUS
DN **133:217693**
TI Remedies for joint diseases
IN Serizawa, Isao; Maekawa, Keisei; Illes, Janos; Neszmeli, Erzsebet
PA Takata **Seiyaku** Co., Ltd., Japan; Richter Gedeon Vegyeszeti Gyar Rt.
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM A61K033-30
ICS A61P019-02; A61P029-00; A61P035-04

CC 1-7 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000053194	A1	20000914	WO 2000-JP1487	20000310

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	EP 1166788	A1	20020102	EP 2000-908017	20000310

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRAI	JP 1999-63718	A	19990310
	WO 2000-JP1487	W	20000310

AB Remedies for joint diseases such as rheumatoid arthritis contain as the active ingredient a complex (assoc.) of **hyaluronic acid** with zinc. Compared with **hyaluronic acid** and zinc (i.e., constituents thereof), this complex synergistically inhibits the proliferation of synovial cells and thus regulates the prodn. of a histoclastic enzyme MMP-9 produced by synovial cells.

ST **antirheumatic** zinc **hyaluronate** MMP 9 inhibitor

IT Eye, disease
(diabetic retinopathy; zinc **hyaluronate** as MMP 9 regulator for treatment of diabetic retinopathy)

IT **Joint, anatomical**
(**disease**; zinc **hyaluronate** for treatment of joint **diseases**)

IT Drug delivery systems
(injections; zinc **hyaluronate** for treatment of joint diseases)

IT Antitumor agents
(metastasis; zinc **hyaluronate** as MMP 9 regulator as antimetastatic agent)

IT **Antirheumatic agents**
(zinc **hyaluronate** for treatment of joint diseases)

IT **146480-36-6, Matrix metalloproteinase** 9
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition in; zinc **hyaluronate** for treatment of joint diseases)

IT **177402-92-5**, Zinc **hyaluronate**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(zinc **hyaluronate** for treatment of joint diseases)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Arthropharm Pty Limited; JP 02502547 A
(2) Arthropharm Pty Limited; CA 1327354 A HCAPLUS
(3) Arthropharm Pty Limited; AU 1545688 A
(4) Arthropharm Pty Limited; EP 356435 A1 HCAPLUS
(5) Arthropharm Pty Limited; DE 3854604 A
(6) Arthropharm Pty Limited; US 5470840 A HCAPLUS
(7) Arthropharm Pty Limited; US 5668116 A HCAPLUS
(8) Arthropharm Pty Limited; WO 8807060 A1 1988 HCAPLUS
(9) Chemical Works Of Gedeon Richter Ltd; JP 03505231 A
(10) Chemical Works Of Gedeon Richter Ltd; CN 1045394 A HCAPLUS

(11) Chemical Works Of Gedeon Richter Ltd; DD 292263 A HCAPLUS
(12) Chemical Works Of Gedeon Richter Ltd; EP 413016 A1 HCAPLUS
(13) Chemical Works Of Gedeon Richter Ltd; AU 5108890 A
(14) Chemical Works Of Gedeon Richter Ltd; HU 53128 A HCAPLUS
(15) Chemical Works Of Gedeon Richter Ltd; US 5472950 A HCAPLUS
(16) Chemical Works Of Gedeon Richter Ltd; ZA 9001357 A HCAPLUS
(17) Chemical Works Of Gedeon Richter Ltd; GR 90100137 A
(18) Chemical Works Of Gedeon Richter Ltd; NO 904584 A
(19) Chemical Works Of Gedeon Richter Ltd; FI 905109 A
(20) Chemical Works Of Gedeon Richter Ltd; IL 93489 A HCAPLUS
(21) Chemical Works Of Gedeon Richter Ltd; KR 9615624 B
(22) Chemical Works Of Gedeon Richter Ltd; WO 9010020 A1 1990 HCAPLUS
(23) Fidia Advanced Biopolymers S R L; JP 11504668 A
(24) Fidia Advanced Biopolymers S R L; AU 695512 B HCAPLUS
(25) Fidia Advanced Biopolymers S R L; DE 69603721 A
(26) Fidia Advanced Biopolymers S R L; EP 827514 A HCAPLUS
(27) Fidia Advanced Biopolymers S R L; IT 95560090 A
(28) Fidia Advanced Biopolymers S R L; WO 9635720 A1 1996 HCAPLUS
IT **146480-36-6, Matrix metalloproteinase** 9
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition in; zinc **hyaluronate** for treatment of joint diseases)
RN 146480-36-6 HCAPLUS
CN Gelatinase B (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **177402-92-5**, Zinc **hyaluronate**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(zinc **hyaluronate** for treatment of joint diseases)
RN 177402-92-5 HCAPLUS
CN Hyaluronic acid, zinc salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L111 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:470317** HCAPLUS
DN **133:94604**
TI Use of polymers as microspheres for wound healing
IN Ritter, Vladimir; Ritter, Marina
PA Polyheal Ltd., Israel
SO U.S., 45 pp., 5861149Cont.-in-part of U.S. 5,861,149.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-74
NCL 424078060
CC **63-7** (Pharmaceuticals)
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6086863	A	20000711	US 1998-177954	19981023
	US 5861149	A	19990119	US 1997-868950	19970604
PRAI	US 1997-868950	A2	19970604		

AB Therapeutic **compns**. of microspheres for application to wounds and/or lesions for accelerating wound healing and muscle regeneration are disclosed. The microspheres are made up of non-biodegradable material having a substantial surface charge. The therapeutic **compn**. further includes a pharmaceutically acceptable carrier in which the microspheres are insol. and a container for holding the **compn**. The therapeutic **compn**. further contains pharmacol. agents or

biologics that accelerate the wound healing process. Microspheres were made of polystyrene, either with carboxyl or amino surface groups or without addnl. surface groups were prepd. The diams. of the microspheres ranged from about 0.1 to about 20 .mu.m. The zeta potential of certain microspheres was also tested and demonstrated that the size of the sphere and the type of surface groups clearly had an effect on the amt. of overall charge carried by each microsphere, which could have important effect on the ability of the microsphere to promote wound healing. Effects of microspheres on collagen synthesis and deposition and on wound healing in humans was shown.

ST wound healing polymer microsphere polystyrene

IT Platelet-derived growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiogenesis; use of polymers as microspheres for wound healing)

IT Skin preparations (pharmaceutical)
(astringents; use of polymers as microspheres for wound healing)

IT Bone, disease
(fracture; use of polymers as microspheres for wound healing)

IT Cytokines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(macrophage-activating factor; use of polymers as microspheres for wound healing)

IT Drug delivery systems
(microspheres; use of polymers as microspheres for wound healing)

IT Drug delivery systems
(ointments; use of polymers as microspheres for wound healing)

IT Ulcer
(stasis; use of polymers as microspheres for wound healing)

IT Bone marrow
(stroma; use of polymers as microspheres for wound healing)

IT Wound
(surgical; use of polymers as microspheres for wound healing)

IT Analgesics
Anesthetics
Antibiotics
Antihistamines
Antitumor agents
Antiviral agents
Cations
Fungicides
Immunostimulants
Pain
Solvents
Wound healing
(use of polymers as microspheres for wound healing)

IT Amino acids, biological studies
Collagens, biological studies
Growth factors, animal
Platelet-derived growth factors
Polymers, biological studies
Polysiloxanes, biological studies
Vitamins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of polymers as microspheres for wound healing)

IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(.beta.-; use of polymers as microspheres for wound healing)

IT **39391-18-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**cyclooxygenase-2**, inhibitors; use of polymers as microspheres for wound healing)

IT 7439-89-6, Iron, biological studies 7439-96-5, Manganese, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ions; use of polymers as microspheres for wound healing)

IT 62229-50-9, Epidermal growth factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(platelet-derived; use of polymers as microspheres for wound healing)

IT 51-43-4, Epinephrine. 57-27-2, Morphine, biological studies 59-46-1, Procaine 60-54-8, Tetracycline 74-79-3, L-Arginine, biological studies 79-57-2, Oxytetracycline 102-60-3, Quadrol 137-58-6, Lidocaine 437-38-7, Fentanyl 561-27-3, Heroin 1403-66-3, Gentamycin 1405-10-3, Neomycin sulfate 1405-20-5, Polymyxin B sulfate 1405-87-4, Bacitracin **9001-92-7**, Proteolytic enzyme. 9002-72-6, GH 9003-21-8, Polymethylacrylate 9003-53-6, Polystyrene 9003-53-6D, Polystyrene, derivs. **9004-61-9**, **Hyaluronic acid** 10102-43-9, Nitric oxide, biological studies 15158-11-9, biological studies 22537-22-0, Magnesium ion, biological studies 22541-53-3, biological studies 23713-49-7, Zinc ion, biological studies 25104-18-1, Polylysine 25619-82-3, Poly-N-ethyl-4-vinyl-pyridinium bromide 38000-06-5, Polylysine 53678-77-6, Muramyl dipeptide 61912-98-9, IGF. 161467-66-9, PF-4
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(use of polymers as microspheres for wound healing)

IT 62031-54-3, Fibroblast growth factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha. and .beta.; use of polymers as microspheres for wound healing)

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Adams; Nature 1985, V318, P533 MEDLINE
(2) Alexander; Mol Cell Biol 1987, V7, P1436 HCAPLUS
(3) Alexandrow; Cancer res 1995, V55, P1452 HCAPLUS
(4) Bommelaer; US 5264207 1993 HCAPLUS
(5) Deckman; US 4380855 1983
(6) Eppley; US 5092883 1992
(7) Gentry; Mol cell Biol 1987, V7, P3418 HCAPLUS
(8) Grosschedl; Cell 1984, V38, P647 HCAPLUS
(9) Hanahan; Nature 1985, V315, P115 HCAPLUS
(10) Haukipuro; ann Surg 1991, V213, P75 MEDLINE
(11) Horton; J Cell Physiol 1989, V141, P8 HCAPLUS
(12) Mann; PNAS 1995, V92, P4502 HCAPLUS
(13) McQuillan; Biochem J 1986, V240, P423 HCAPLUS
(14) Meisner; US 4772591 1988 HCAPLUS
(15) Mescher; J Immunol 1992, V149, P2402 HCAPLUS
(16) Momaerts; Proc Natl Acad Sci 1991, V88, P3084
(17) Ornitz; Cold Spring Harbor Symp 1986, V50, P399
(18) Osborn; J Orthop Res 1989, V7, P35 HCAPLUS
(19) Rosen; J cell Physiol 1988, V134, P337 HCAPLUS
(20) Selden; Science 1987, V236, P714 HCAPLUS
(21) Shani; Nature 1985, V314, P283 HCAPLUS

(22) Shlomo, M; Reactive Polymers 1983, V1, P241
(23) Soon-Shiong; US 5700848 1997 HCAPLUS
(24) Swift; cell 1984, V38, P639 HCAPLUS
(25) Tardy; US 4931546 1990 HCAPLUS
(26) Thompson; Invest Radiol 1991, V26, P604
(27) Weisz; US 5658894 1997 HCAPLUS

IT **39391-18-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**cyclooxygenase-2**, inhibitors; use of polymers as microspheres for wound healing)
RN 39391-18-9 HCAPLUS
CN Synthetase, prostaglandin endoperoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **9001-92-7**, Proteolytic enzyme. **9004-61-9**, **Hyaluronic acid**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(use of polymers as microspheres for wound healing)
RN 9001-92-7 HCAPLUS
CN Proteinase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI,. 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L111 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:34995** HCAPLUS
DN **132:102856**
TI **Hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-associated diseases
IN Prestwich, Glenn D.; Ziebell, Michael; Luo, Bai; Zhao, Zhan-Gong
PA USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q
CC **1-12** (Pharmacology)
Section cross-reference(s): **63**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000001841	A2	20000113	WO 1999-US15263	19990706
WO 2000001841	A3	20011108		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2346742	AA	20000113	CA 1999-2346742	19990706
AU 9949716	A1	20000124	AU 1999-49716	19990706
EP 1169048	A2	20020109	EP 1999-933718	19990706

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRAI US 1998-91758P	P	19980706	
US 1999-347707	A	19990703	

WO 1999-US15263 W 19990706

AB HA mimics and methods related thereto are disclosed. In particular, mimics with structures detd. by virtue of novel methods, and the novel methods are disclosed. The HA mimics are useful for a variety of HA-related uses, including treatment of inflammatory diseases, tumor angiogenesis, skin disease, bone disease, and cardiovascular diseases.

ST **hyaluronate** mimic sequence antiinflammatory antitumor angiogenesis

IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(H-CAM (homing cell adhesion mol.); **hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(RHAMM (receptor for **hyaluronic acid**-mediated motility); **hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)

IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(TSG-6; **hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)

IT Neoplasm
(angiogenesis in; **hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)

IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antireceptor; **hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)

IT Cardiovascular system
(disease; **hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)

IT Immunity
(disorder; **hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)

IT Anti-inflammatory agents
Antiarthritics
Antibiotics
Antirheumatic agents
Bone, disease
Immobilization, biochemical
Infection
Inflammation
Osteoarthritis
Peptide library
Phage display library
Protein sequences
Rheumatoid arthritis
Skin, disease
Wound healing
Wound healing promoters
(**hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)

IT CD44 (antigen)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)

IT Antitumor agents
(metastasis; **hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)
IT Angiogenesis
(tumor; **hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)
IT **9004-61-9D, Hyaluronic acid,** analogs
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(**hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)
IT 180731-61-7P 254965-30-5P 254965-31-6P 254965-32-7P 254965-33-8P
254965-34-9P 254965-35-0P 254965-36-1P 254965-37-2P 254965-38-3P
254965-39-4P 254965-40-7P 254965-41-8P 254965-42-9P 254965-43-0P
254965-44-1P 254965-45-2P 254965-46-3P 254965-47-4P 254965-48-5P
254965-49-6P 254965-50-9P 254965-51-0P 254965-52-1P 254965-53-2P
254965-54-3P 254965-55-4P 254965-56-5P 254965-57-6P 254965-58-7P
254965-59-8P 255057-60-4P 255057-68-2P 255057-71-7P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)
IT **9004-61-9D, Hyaluronic acid,** analogs
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(**hyaluronic acid** mimics for treatment of inflammation and other **hyaluronate**-assocd. diseases)
RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L111 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:783929** HCAPLUS
DN **132:18780**
TI Compositions comprising antimicrotubule agents for treating or preventing inflammatory diseases
IN Hunter, William L.
PA Angiotech Pharmaceuticals, Inc., Can.
SO PCT Int. Appl., 340 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-335
ICS A61K031-425; A61K031-365; A61K031-045; A61K031-505; A61K033-16; A61K031-40; A61K031-22
CC 1-7 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9962510	A2	19991209	WO 1999-CA464	19990601

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	US 6495579	B1	20021217	US 1998-88546	19980601
PRAI	US 1998-88546	A	19980601		
	US 1996-32215P	P	19961202		
	US 1997-63087P	P	19971024		
	US 1997-980549	A2	19971201		

AB Methods and compns. for treating or preventing inflammatory diseases, e.g. psoriasis or multiple sclerosis, are provided, comprising the step of delivering to the site of inflammation an antimicrotubule agent, or analog or deriv. thereof.

ST antimicrotubule agent inflammation treatment; microtubule antimicrotubule agent inflammation treatment

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AP-1 (activator protein 1); antimicrotubule agents for treating or preventing inflammatory diseases)

IT mRNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MMP-1 and MMP-3; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-.kappa.B (nuclear factor .kappa.B); antimicrotubule agents for treating or preventing inflammatory diseases)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Shiga-like toxin; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Cell proliferation
(T cell; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Neutrophil
(activation; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Connective tissue
Surgery
(adhesions; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Medical goods
(antimicrotubule agent-coated; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Adhesion, biological
Angiogenesis inhibitors
Anti-inflammatory agents
Antiarthritics
Antitumor agents
Astrocyte
Cytotoxic agents
Drug delivery systems
Micelles
Microtubule
Neutrophil
Permeation enhancers
Psoriasis
Transplant rejection
(antimicrotubule agents for treating or preventing inflammatory diseases)

IT Diterpenes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(antimicrotubule agents for treating or preventing inflammatory diseases)

IT Aggrecans
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antimicrotubule agents for treating or preventing inflammatory diseases)

IT Albumins, biological studies
Fibronectins
Gelatins, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polyurethanes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimicrotubule agents for treating or preventing inflammatory diseases)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(block, diblock; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(block, triblock; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Medical goods
(catheters, indwelling, antimicrotubule agent-coated; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Neutrophil
(degranulation; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Periodontium
(disease; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Blood vessel
(endothelium; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Drug delivery systems
(films; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Drug delivery systems
(gels; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Prosthetic materials and Prosthetics
(implants, vascular, antimicrotubule agent-coated; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Lung, disease
(inflammation; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Intestine, disease
(inflammatory; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Skin
(keratinocyte; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Drug delivery systems
(microcapsules, nylon microcapsules; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Drug delivery systems
(microparticles; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Drug delivery systems
(nasal; antimicrotubule agents for treating or preventing inflammatory diseases)

IT Prostate gland
Prostate gland
(neoplasm, inhibitors; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Cell activation
Cell degranulation
(neutrophil; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Polyamides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nylon microcapsules; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Drug delivery systems
(ointments; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Drug delivery systems
(oral; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Drug delivery systems
(pastes; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Kidney, disease
(polycystic; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Glycols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymers; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Nose
(polyp; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Proliferation inhibition
(proliferation inhibitors; antimicrotubule agents for treating or preventing inflammatory diseases)
IT T cell (lymphocyte)
(proliferation; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Antitumor agents
(prostate gland; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Artery, disease
(restenosis; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Cartilage
Shark
(shark cartilage powder; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Drug delivery systems
(sprays, nanospray; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Artery, disease
(stenosis; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Medical goods
(stents, antimicrotubule agent-coated; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Protamines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(sulfates, tetrahydro; antimicrotubule agents for treating or preventing inflammatory diseases)
IT **Synovial membrane**
(synoviocyte; antimicrotubule agents for treating or preventing

inflammatory diseases)
IT Lupus erythematosus
(systemic; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Multiple sclerosis
(therapeutic agents; antimicrotubule agents for treating or preventing inflammatory diseases)
IT Drug delivery systems
(topical; antimicrotubule agents for treating or preventing inflammatory diseases)
IT 50-04-4 52-21-1 57-22-7 59-05-2 64-86-8 145-63-1 446-72-0 865-21-4, Vincaleukoblastine 7689-03-4 9050-30-0D, fragments 10540-29-1 27774-13-6 37353-31-4, Vanadate 38213-69-3 52205-73-9 63177-57-1 66107-60-6 77699-47-9, Herbimycin **86102-31-0** 100827-28-9 144676-04-0 174882-69-0, Pycnogenol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antimicrotubule agents for treating or preventing inflammatory diseases)
IT 69-33-0 69-33-0D, derivs. 107-41-5 107-41-5D, derivs. 459-73-4 459-73-4D, derivs. 7784-18-1, Aluminum fluoride (AlF3) 7784-18-1D, Aluminum fluoride (AlF3), derivs. 7789-20-0, Water-d2 7789-20-0D, Water-d2, derivs. 33069-62-4 33069-62-4D, derivs. 85419-94-9 85419-94-9D, derivs. 127943-53-7 127943-53-7D, derivs. 149550-36-7 149550-36-7D, derivs. 152044-53-6 152044-53-6D, derivs. 152044-54-7 152044-54-7D, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimicrotubule agents for treating or preventing inflammatory diseases)
IT **9001-12-1**, Collagenase 11062-77-4, Superoxide **79955-99-0**, Stromelysin 1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antimicrotubule agents for treating or preventing inflammatory diseases)
IT 1338-43-8 7585-39-9D, .beta.-Cyclodextrin, Hydroxypropyl derivs. 9002-89-5 9003-01-4 9004-54-0, Dextran, biological studies 9004-57-3 **9004-61-9D, Hyaluronic acid**, crosslinked 9004-64-2 9004-67-5 9011-14-7 9012-76-4, Chitosan 9012-76-4D, Chitosan, crosslinked 17465-86-0, .gamma.-Cyclodextrin 17465-86-0D, .gamma.-Cyclodextrin, Hydroxypropyl derivs. 24937-78-8 24980-41-4 25104-18-1 25248-42-4, Poly[oxy(1-oxo-1,6-hexanediyl)] 25322-68-3 34346-01-5 38000-06-5 80137-67-3 106392-12-5 119388-27-1 188360-48-7 250580-74-6 251911-63-4 251911-67-8 263237-87-2
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(antimicrotubule agents for treating or preventing inflammatory diseases)
IT 57-55-6, 1,2-Propanediol, biological studies 64-17-5, Ethanol, biological studies 110-27-0 111-90-0 112-80-1, 9-Octadecenoic acid (9Z)-, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(permeation enhancer; antimicrotubule agents for treating or preventing inflammatory diseases)
IT **86102-31-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antimicrotubule agents for treating or preventing inflammatory diseases)
RN 86102-31-0 HCAPLUS
CN Proteinase inhibitor, TIMP (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9001-12-1**, Collagenase **79955-99-0**, Stromelysin 1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antimicrotubule agents for treating or preventing inflammatory diseases)
RN 9001-12-1 HCAPLUS
CN Collagenase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 79955-99-0 HCAPLUS
CN Stromelysin 1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9004-61-9D, Hyaluronic acid**, crosslinked
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(antimicrotubule agents for treating or preventing inflammatory diseases)
RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L111 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:753089** HCAPLUS
DN **131:356137**
TI Pharmaceuticals complexed with **hyaluronic acid** for diseases of the joints
IN **Tamura, Tatsuya; Okamachi, Akira**
PA **Chugai Seiyaku Kabushiki Kaisha**, Japan
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM A61K031-725
ICS C08B037-08; A61K045-00; A61K031-725; A61K031-40
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9959603	A1	19991125	WO 1999-JP2600	19990519 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2332802	AA	19991125	CA 1999-2332802	19990519 <--
	AU 9938490	A1	19991206	AU 1999-38490	19990519 <--
	AU 752280	B2	20020912		
	EP 1082963	A1	20010314	EP 1999-921167	19990519 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	JP 1998-138329	A	19980520 <--		
	JP 1998-224187	A	19980807 <--		
	JP 1999-43064	A	19990222 <--		
	WO 1999-JP2600	W	19990519 <--		

APP

AB Complexes of a pharmaceutical with **hyaluronic acid** or deriv. thereof, are prepd. for inserting the pharmaceutical to the glenoid cavities. For example, one or more pharmaceutical such as matrix **proteinase** inhibitor is bound to **hyaluronic acid** or its deriv. The medications are useful in treating chronic joint rheumatism.

ST joint disease pharmaceutical **hyaluronate** complex

IT **Joint, anatomical**
(**disease**; pharmaceutical-**hyaluronate** complexes for treatment of)

IT Drugs
Rheumatic diseases
(**hyaluronate**-pharmaceutical complexes for treatment of diseases in bone joints)

IT **9001-92-7D, Proteinase**, inhibitor, complex with **hyaluronate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for treatment of diseases in bone joints)

IT **9004-61-9, Hyaluronic acid 9004-61-9D , Hyaluronic acid**, derivs.
RL: **BUU (Biological use, unclassified)**; BIOL (Biological study); **USES (Uses)**
(**hyaluronate**-pharmaceutical complexes for treatment of diseases in bone joints)

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; EP 216453 A HCAPLUS
(2) Anon; US 4851521 A HCAPLUS
(3) Anon; US 4965353 A HCAPLUS
(4) Anon; US 5202431 A HCAPLUS
(5) Anon; US 5336767 A HCAPLUS
(6) Anon; US 5773438 A HCAPLUS
(7) Anon; US 5892112 A HCAPLUS
(8) Anon; EP 690841 A HCAPLUS
(9) Anon; WO 95/199965 A1
(10) Fidia, S; JP 62-64802 A 1987 HCAPLUS
(11) Glycomed Inc; JP 09-501183 A 1997
(12) Vasilionkaitis, V; Sint Izuch Fiziol Akt Veshchestv Tezisy Dokl Mezhvuz Nauchn Konf Uchastiem Farmakol Latv Est SSR 1975, P20 HCAPLUS

IT **9001-92-7D, Proteinase**, inhibitor, complex with **hyaluronate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for treatment of diseases in bone joints)

RN 9001-92-7 HCAPLUS
CN Proteinase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **9004-61-9, Hyaluronic acid 9004-61-9D , Hyaluronic acid**, derivs.
RL: **BUU (Biological use, unclassified)**; BIOL (Biological study); **USES (Uses)**
(**hyaluronate**-pharmaceutical complexes for treatment of diseases in bone joints)

RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L111 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS

AN **1999:648783** HCAPLUS
DN **131:252570**
TI Local drug preparations containing **hyaluronate** salt and soluble antiinflammatory agents for treatment of chronic rheumatism
IN Baba, Takaaki
PA Shiseido Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K031-725
ICS A61K031-725; A61K009-08; A61K031-56; A61K045-00
CC **1-7** (Pharmacology)
Section cross-reference(s): **63**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 11279065	A2	19991012	JP 1998-96901	19980325
PRAI JP 1998-96901		19980325		

AB Local drug prepns. contg. **hyaluronic acid** and its salts and sol. steroidal and nonsteroidal antiinflammatory agents are claimed for treatment of chronic rheumatism. Examples of topical injections sterilized by filtration were given.
ST topical **hyaluronate** antiinflammatory rheumatism
IT Drug delivery systems
(injections; local drug prepns. contg. **hyaluronate** salt and sol. antiinflammatory agents for treatment of chronic rheumatism)
IT Anti-inflammatory agents
Antirheumatic agents
Drug interactions
(local drug prepns. contg. **hyaluronate** salt and sol. antiinflammatory agents for treatment of chronic rheumatism)
IT Steroids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(local drug prepns. contg. **hyaluronate** salt and sol. antiinflammatory agents for treatment of chronic rheumatism)
IT Anti-inflammatory agents
(nonsteroidal; local drug prepns. contg. **hyaluronate** salt and sol. antiinflammatory agents for treatment of chronic rheumatism)
IT Drug delivery systems
(topical; local drug prepns. contg. **hyaluronate** salt and sol. antiinflammatory agents for treatment of chronic rheumatism)
IT 54-21-7, Sodium salicylate 2392-39-4, Dexamethasone sodium phosphate **9004-61-9, Hyaluronic acid 9067-32-7**, Sodium **hyaluronate**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(local drug prepns. contg. **hyaluronate** salt and sol. antiinflammatory agents for treatment of chronic rheumatism)
IT **9004-61-9, Hyaluronic acid 9067-32-7**, Sodium **hyaluronate**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(local drug prepns. contg. **hyaluronate** salt and sol. antiinflammatory agents for treatment of chronic rheumatism)
RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9067-32-7 HCAPLUS
CN Hyaluronic acid, sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L111 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1997:47282** HCAPLUS
DN **126:84211**
TI Anti-tumor activity of the dual **cyclooxygenase**-1/2 inhibitor diclofenac in **combination** with **hyaluronan**
AU Seed, M. P.; Freemantle, C. N.; Papworth, J.; Brown, J. R.; Willoughby, D. A.
CS Medical College, Saint Bartholomew's Hospital, London, ECIM 6BQ, UK
SO Round Table Series - Royal Society of Medicine Press (1996), 45(Fourth International Workshop on Hyaluronan in Drug Delivery, 1996), 59-67
CODEN: RTMPFO
PB Royal Society of Medicine Press
DT Journal
LA English
CC **1-6** (Pharmacology)
AB Diclofenac dose-dependently inhibited the growth of colon-26 murine adenocarcinoma cell proliferation and the action of diclofenac was not affected by **hyaluronan** at 1 .mu.g/mL. The role of inhibition of **cyclooxygenase**-1/2 by diclofenac in its antitumor action is discussed.
ST diclofenac **hyaluronan** colon carcinoma inhibitor; cyclooxygenase diclofenac antitumor colon carcinoma
IT Antitumor agents
(antitumor activity of the dual **cyclooxygenase**-1/2 inhibitor diclofenac in **combination** with **hyaluronan**)
IT Antitumor agents
(colon carcinoma; antitumor activity of the dual **cyclooxygenase**-1/2 inhibitor diclofenac in **combination** with **hyaluronan**)
IT Intestine, neoplasm
(colon, carcinoma, inhibitors; antitumor activity of the dual **cyclooxygenase**-1/2 inhibitor diclofenac in **combination** with **hyaluronan**)
IT **9004-61-9, Hyaluronan** 15307-86-5, Diclofenac
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(antitumor activity of the dual **cyclooxygenase**-1/2 inhibitor diclofenac in **combination** with **hyaluronan**)
IT **39391-18-9, Cyclooxygenase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antitumor activity of the dual **cyclooxygenase**-1/2 inhibitor diclofenac in **combination** with **hyaluronan**)
IT **9004-61-9, Hyaluronan**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(antitumor activity of the dual **cyclooxygenase**-1/2 inhibitor diclofenac in **combination** with **hyaluronan**)
RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

not a conjugate

IT **39391-18-9, Cyclooxygenase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antitumor activity of the dual **cyclooxygenase**-1/2 inhibitor diclofenac in **combination** with **hyaluronan**)
RN 39391-18-9 HCAPLUS
CN Synthetase, prostaglandin endoperoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L111 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1995:364299** HCAPLUS
DN **122:115054**
TI Purified natural and synthetic compounds for the treatment of osteoarthritis
IN Lansbury, Peter T., Jr.; Hauschka, Peter V.
PA Neogenix, Inc., USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-165
ICS A61K031-075; A61K031-235; A61K031-215; A61K031-655; A61K031-715; A61K031-725; A61K031-73; A61K031-735; C07H003-06; C07H007-033; C07H013-02; C08B037-10; C07C015-20; C07C015-24; C07C015-27; C07C211-43; C07C211-54; C07C225-02; C07C233-01
CC **63-7** (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9428889	A1	19941222	WO 1994-US6490	19940608
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, UA, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9472058	A1	19950103	AU 1994-72058	19940608
PRAI US 1993-73189		19930608		
WO 1994-US6490		19940608		

AB The present invention relates to individual, well-defined compds. and the uses of these compds., alone or in conjunction with bioactive mols. such as growth factors or **metalloproteinase** inhibitors, for the repair of cartilage damage as, for example, is found in osteoarthritis. Such well-defined compds. may include purified components of the extracellular **matrix**, derivs. of extracellular **matrix** components, and glycosaminoglycan mimics. The glycosaminoglycan mimics include chondroitin-4-sulfate, chondroitin-6-sulfate, **hyaluronic acid**, heparin, heparan sulfate, keratan sulfate, dermatan sulfate, poly-N-acetylglucosamine, and poly-N-glucosamine.
ST extracellular matrix glycosaminoglycan osteoarthritis
IT Animal growth regulators
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(connective tissue-activating; glycosaminoglycan and bioactive mol. **combinations** for treatment of osteoarthritis)
IT **Cartilage**
Extracellular matrix
(extracellular matrix components for treatment of osteoarthritis)
IT Glycosaminoglycans, biological studies
Proteoglycans, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(extracellular matrix components for treatment of osteoarthritis)
IT **Chondrocyte**
(screening of glycosaminoglycans for their ability to repair damaged

cartilage)
IT Inflammation inhibitors
(antiarthritics, extracellular matrix components for treatment of osteoarthritis)
IT Animal growth regulators
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blood platelet-derived growth factors, glycosaminoglycan and bioactive mol. **combinations** for treatment of osteoarthritis)
IT 145-63-1, Suramin 573-58-0, Congo red **9004-61-9**, **Hyaluronic acid** 9005-49-6, Heparin, biological studies 9050-30-0, Heparan sulfate 9056-36-4, Keratan sulfate 24967-93-9, Chondroitin-4-sulfate 24967-94-0, Dermatan sulfate 25322-46-7, Chondroitin-6-sulfate 27555-50-6 35110-26-0, Polyglucosamine
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(extracellular matrix components for treatment of osteoarthritis)
IT 61912-98-9, Insulin-like growth factor 62031-54-3, Cartilage-derived growth factor 105844-41-5, Plasminogen activator inhibitor **124861-55-8**, TIMP2 **140208-24-8**, TIMP1 **145266-99-5**, **Metalloproteinase** inhibitor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycosaminoglycan and bioactive mol. **combinations** for treatment of osteoarthritis)
IT 7782-77-6, Nitrous acid 9001-06-3, Chitinase 9024-13-9, Chondroitinase ABC 9025-39-2, Heparinase 9047-57-8, Chondroitinase AC
RL: NUU (Other use, unclassified); USES (Uses)
(purifn. of extracellular matrix for use in repair of damaged cartilage)
IT **9004-61-9**, **Hyaluronic acid**
RL: **THU (Therapeutic use)**; BIOL (Biological study); **USES (Uses)**
(extracellular matrix components for treatment of osteoarthritis)
RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **124861-55-8**, TIMP2 **140208-24-8**, TIMP1 **145266-99-5**, **Metalloproteinase** inhibitor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycosaminoglycan and bioactive mol. **combinations** for treatment of osteoarthritis)
RN 124861-55-8 HCAPLUS
CN Proteinase inhibitor, TIMP 2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 140208-24-8 HCAPLUS
CN Proteinase inhibitor, TIMP 1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 145266-99-5 HCAPLUS
CN Proteinase inhibitor, metallo- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L111 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS
AN **1994:236174** HCAPLUS
DN **120:236174**
TI Use of lipid-**bound** glycosaminoglycans for the treatment of rheumatoid arthritis
IN Aoki, Shigehisa; Iwasaki, Shinichi; Sugiura, Nobuo; Suzuki, Sakaru; Kimata, Koji
PA Seikagaku Corp., Japan
SO Eur. Pat. Appl., 26 pp.

CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K031-735
CC **1-7** (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 581282	A1	19940202	EP 1993-112169	19930729
	EP 581282	B1	19990512		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 06072893	A2	19940315	JP 1992-203558	19920730
	CA 2101482	AA	19940131	CA 1993-2101482	19930728
	AU 9344314	A1	19940203	AU 1993-44314	19930729
	AU 668963	B2	19960523		
	US 5470578	A	19951128	US 1993-98936	19930729
	AT 179892	E	19990515	AT 1993-112169	19930729
PRAI	JP 1992-203558		19920730		

AB A lipid-**bound** glycosaminoglycan is prepd. as an **antirheumatic** agent to prevent the extension of pannus. For example, **hyaluronic acid** was partially oxidized, lactonized, and **reacted** with dipalmitoylphosphatidylethanolamine (PE) to give a PE-**bound hyaluronic acid**. Inhibitory effect of the PE-**bound hyaluronic acid** on extension of pannus in **simultaneous** organ culture of rabbit articular cartilage tissue and synovial membrane tissue was demonstrated.

ST lipid **bound** glycosaminoglycan rheumatoid arthritis treatment; **antirheumatic hyaluronate** phosphatidylethanolamine **conjugate**

IT Phosphatidylserines
RL: BIOL (Biological study)
(C16-18, **conjugates** with chondroitin sulfate, as **antirheumatic** agents)

IT Inflammation inhibitors
(antiarthritics, lipid-**bound** glycosaminoglycans for)

IT **Inflammation inhibitors**
(**antirheumatics**, lipid-**bound** glycosaminoglycans as)

IT **Synovial membrane**
(disease, pannus, extension of, in arthritis, prevention of, lipid-**bound** glycosaminoglycans for)

IT Lipids, compounds
Phospholipids, compounds
RL: BIOL (Biological study)
(glycero-, **reaction** products, with glycosaminoglycans, **antirheumatic** activity of)

IT Pharmaceutical dosage forms
(injections, intraarticular, lipid-**bound** glycosaminoglycans in, for treatment of rheumatoid arthritis)

IT Lipids, compounds
Phosphatidylethanolamines
Phosphatidylserines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**reaction** products, **antirheumatic*** activity **ofPhosphatidylethanolaminesnog**)

IT Glycosaminoglycans, compounds
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**reaction** products, with lipids, **antirheumatic** activity of)

IT **9004-61-9, Hyaluronic acid** 9005-49-6,
Heparin, **reactions** 9007-27-6, Chondroitin 9007-28-7,

Chondroitin sulfate 9050-30-0, Heparan sulfate 24967-94-0, Dermatan sulfate
RL: BIOL (Biological study)
(partial oxidn. and lactonization of, in prepn. of **antirheumatic** lipid **conjugates**)

IT 154275-57-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and **reaction** of, with aminated chondroitin sulfate)

IT 28474-99-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and **reaction** of, with imides)

IT 3026-45-7DP, Dipalmitoylphosphatidylethanolamine, **reaction** products with **hyaluronate 9004-61-9DP**, **Hyaluronic acid**, lactones, **reaction** products with dipalmitoylphosphatidylethanolamine 9007-28-7DP, Chondroitin sulfate, lactones, **reaction** products with stearoylpalmitoylphosphatidylserine 154275-57-7DP, **reaction** products with aminated chondroitin sulfate
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antirheumatic** agent)

IT 108-30-5, Succinic anhydride, **reactions**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**reaction** of, with glyceryl monostearate)

IT 31566-31-1, Glyceryl monostearate
RL: RCT (Reactant); RACT (Reactant or reagent)
(**reaction** of, with succinic anhydride)

IT **9004-61-9**, **Hyaluronic acid**
RL: BIOL (Biological study)
(partial oxidn. and lactonization of, in prepn. of **antirheumatic** lipid **conjugates**)

RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **9004-61-9DP**, **Hyaluronic acid**, lactones, **reaction** products with dipalmitoylphosphatidylethanolamine
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antirheumatic** agent)

RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> fil reg
FILE 'REGISTRY' ENTERED AT 17:14:09 ON 21 JAN 2003
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 20 JAN 2003 HIGHEST RN 479577-81-6
DICTIONARY FILE UPDATES: 20 JAN 2003 HIGHEST RN 479577-81-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

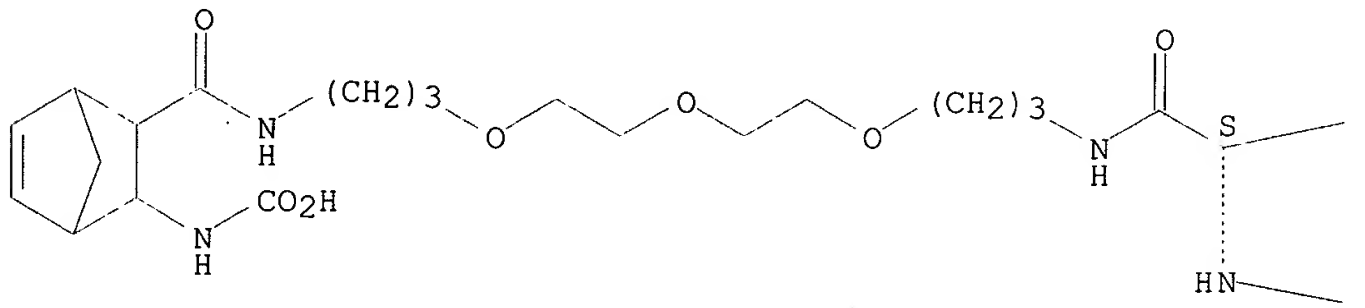
Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can tot

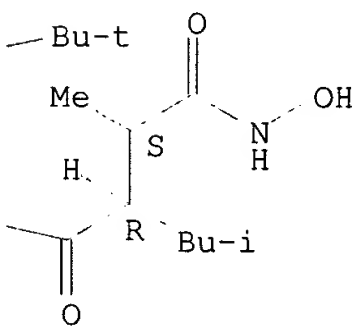
L112 ANSWER 1 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **434283-21-3** REGISTRY
CN Carbamic acid, [3-[(18S,21R)-18-(1,1-dimethylethyl)-21-[(1S)-2-(hydroxyamino)-1-methyl-2-oxoethyl]-23-methyl-1,17,20-trioxo-6,9,12-trioxa-2,16,19-triazatetracos-1-yl]bicyclo[2.2.1]hept-5-en-2-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H59 N5 O10
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

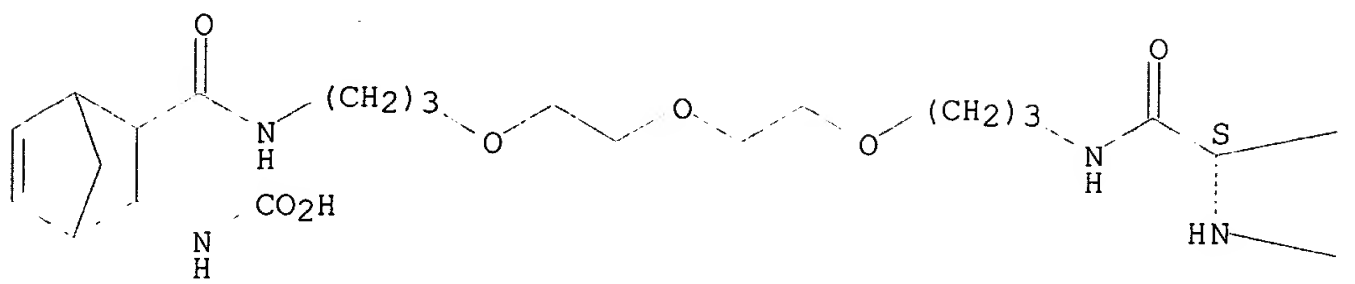
REFERENCE 1: 137:24315

L112 ANSWER 2 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **434283-20-2** REGISTRY
CN Carbamic acid, [3-[(18S,21R)-18-(1,1-dimethylethyl)-21-[2-(hydroxyamino)-2-oxoethyl]-23-methyl-1,17,20-trioxo-6,9,12-trioxa-2,16,19-triazatetracos-1-

yl]bicyclo[2.2.1]hept-5-en-2-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H57 N5 O10
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



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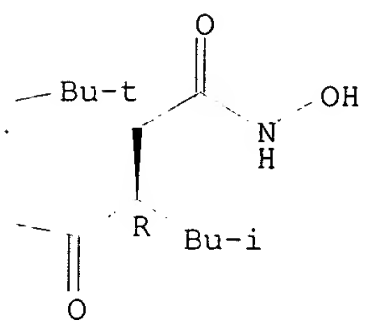

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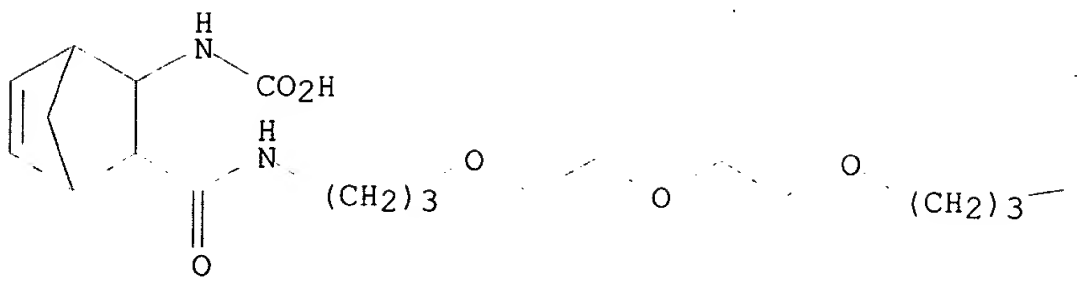
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:24315

L112 ANSWER 3 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **434283-19-9** REGISTRY
CN Carbamic acid, [3-[17-[(6S,7R,10S)-6-[(hydroxyamino)carbonyl]-7-(2-methylpropyl)-8-oxo-2-oxa-9-azabicyclo[10.2.2]hexadeca-12,14,15-trien-10-yl]-1,17-dioxo-6,9,12-trioxa-2,16-diazaheptadec-1-yl]bicyclo[2.2.1]hept-5-en-2-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C39 H59 N5 O11**
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



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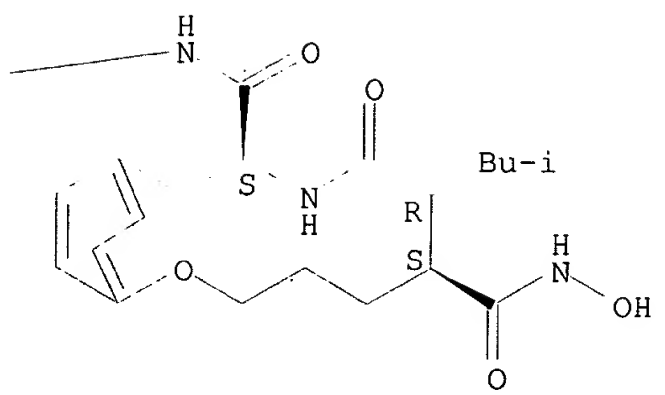


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

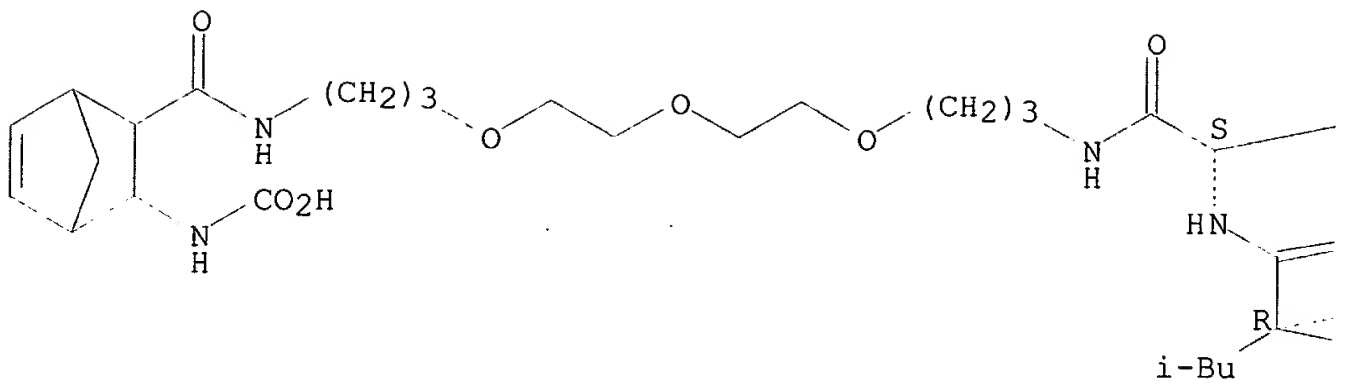
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:24315

L112 ANSWER 4 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **434283-18-8** REGISTRY
CN Carbamic acid, [3-[(18S,21R,22S)-18-(1,1-dimethylethyl)-22-[(hydroxyamino)carbonyl]-21-(2-methylpropyl)-1,17,20-trioxo-6,9,12,23-tetraoxa-2,16,19-triazatetracos-1-yl]bicyclo[2.2.1]hept-5-en-2-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H59 N5 O11
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



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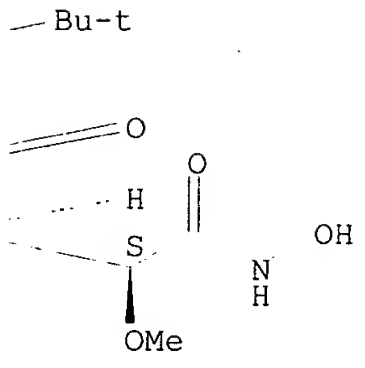


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

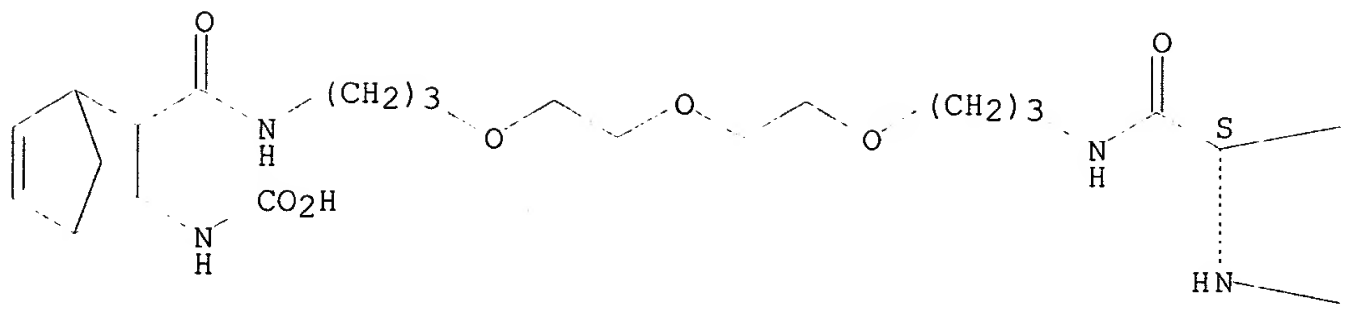
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:24315

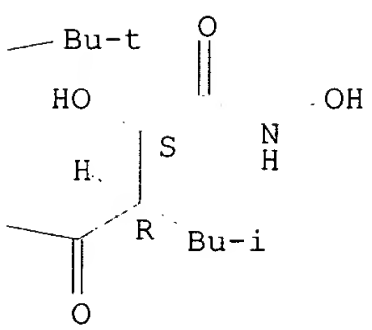
L112 ANSWER 5 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **434283-17-7** REGISTRY
CN Carbamic acid, [3-[(18S,21R)-18-(1,1-dimethylethyl)-21-[(1S)-1-hydroxy-2-(hydroxyamino)-2-oxoethyl]-23-methyl-1,17,20-trioxo-6,9,12-trioxa-2,16,19-triazatetracos-1-yl]bicyclo[2.2.1]hept-5-en-2-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H57 N5 O11
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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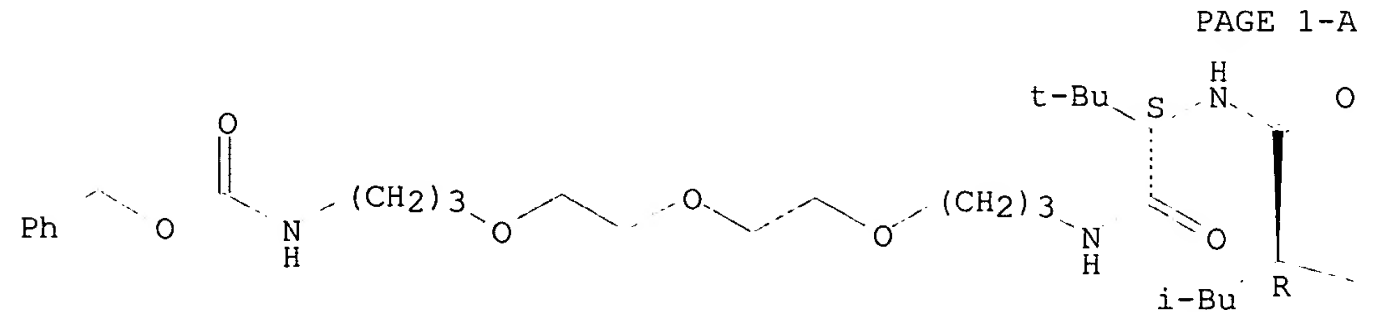
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:24315

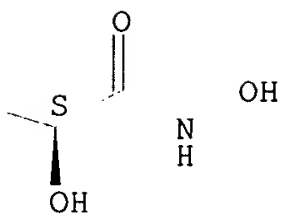
L112 ANSWER 6 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **433708-37-3** REGISTRY
CN 6,9,12-Trioxa-2,16,19-triazatetracosanoic acid, 18-(1,1-dimethylethyl)-21-[(1S)-1-hydroxy-2-(hydroxyamino)-2-oxoethyl]-23-methyl-17,20-dioxo-, phenylmethyl ester, (18S,21R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H54 N4 O10
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:24315

L112 ANSWER 7 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **177402-92-5** REGISTRY
CN Hyaluronic acid, zinc salt (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Curiosin
CN Zinc hyaluronate
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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15 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:44739

REFERENCE 2: 137:333054

REFERENCE 3: 137:268441

REFERENCE 4: 136:369236

REFERENCE 5: 136:221741

REFERENCE 6: 135:92794

REFERENCE 7: 135:86710

REFERENCE 8: 134:9354

REFERENCE 9: 133:217693

REFERENCE 10: 133:125288

L112 ANSWER 8 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **146480-36-6** REGISTRY
CN Gelatinase B (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 92,000-Mol.-wt. gelatinase

CN 92,000-Mol.-wt. type IV collagenase
CN 92-kD Gelatinase
CN 92-kDa Gelatinase
CN 92-kDa Type IV collagenase
CN 95 kDa Type IV collagenase/gelatinase
CN Collagenase IV
CN Collagenase type IV
CN E.C. 3.4.24.35
CN Gelatinase MMP 9
CN Matrix metalloprotease 9
CN Matrix metalloproteinase 9
CN MMP 9
CN Type IV collagen metalloproteinase
CN Type IV collagenase
CN Type IV collagenase/gelatinase
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2950 REFERENCES IN FILE CA (1962 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2966 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:37954

REFERENCE 2: 138:37789

REFERENCE 3: 138:37771

REFERENCE 4: 138:37566

REFERENCE 5: 138:37447

REFERENCE 6: 138:37394

REFERENCE 7: 138:37277

REFERENCE 8: 138:37107

REFERENCE 9: 138:37069

REFERENCE 10: 138:36911

L112 ANSWER 9 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **146480-35-5** REGISTRY
CN Gelatinase A (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 72 kDa Gelatinase
CN 72 kDa Gelatinase type A
CN 72,000-Mol.-wt. gelatinase
CN 72,000-Mol.-wt. type IV collagenase
CN Collagenase IV
CN Collagenase type IV
CN E.C. 3.4.24.24
CN Matrix metalloprotease 2
CN Matrix metalloproteinase 2
CN MMP 2
CN Type IV collagen metalloproteinase
CN Type IV collagenase
CN Type IV collagenase/gelatinase

MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
3127 REFERENCES IN FILE CA (1962 TO DATE)
11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3143 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:37771

REFERENCE 2: 138:37164

REFERENCE 3: 138:37119

REFERENCE 4: 138:37069

REFERENCE 5: 138:36964

REFERENCE 6: 138:36862

REFERENCE 7: 138:36820

REFERENCE 8: 138:36590

REFERENCE 9: 138:36281

REFERENCE 10: 138:35169

L112 ANSWER 10 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **145266-99-5** REGISTRY
CN Proteinase inhibitor, metallo- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Metalloprotease inhibitor
CN Metalloproteinase inhibitor
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CIN, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
90 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
91 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:346178

REFERENCE 2: 137:322841

REFERENCE 3: 137:121462

REFERENCE 4: 136:319368

REFERENCE 5: 136:290000

REFERENCE 6: 136:227913

REFERENCE 7: 136:131785

REFERENCE 8: 136:49642

REFERENCE 9: 136:31664

REFERENCE 10: 136:1566

L112 ANSWER 11 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **141907-41-7** REGISTRY
CN Proteinase, matrix metallo- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Matrix metalloendoproteinase
CN Matrix metalloprotease
CN Matrix metalloprotease HIPHUM35
CN Matrix metalloproteinase
CN Matrix-degrading metalloproteinase
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CHEMCATS, CIN, PROMT, TOXCENTER, USPAT2, USPATFULL

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2230 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:37992

REFERENCE 2: 138:37981

REFERENCE 3: 138:37447

REFERENCE 4: 138:36719

REFERENCE 5: 138:36683

REFERENCE 6: 138:35680

REFERENCE 7: 138:35169

REFERENCE 8: 138:35094

REFERENCE 9: 138:22909

REFERENCE 10: 138:22681

L112 ANSWER 12 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **140208-24-8** REGISTRY
CN Proteinase inhibitor, TIMP 1 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN TIMP 1
CN Tissue inhibitor of metalloproteinase-1
MF Unspecified
CI MAN
SR CA
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL

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1635 REFERENCES IN FILE CA (1962 TO DATE)
33 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1644 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:37164

REFERENCE 2: 138:37027

REFERENCE 3: 138:33034

REFERENCE 4: 138:32929

REFERENCE 5: 138:23404

REFERENCE 6: 138:23009

REFERENCE 7: 138:22812

REFERENCE 8: 138:21264

REFERENCE 9: 138:12378

REFERENCE 10: 138:11772

L112 ANSWER 13 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **124861-55-8** REGISTRY
CN Proteinase inhibitor, TIMP 2 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN TIMP 2
CN TIMP-2 proteinase inhibitor
CN Tissue inhibitor metalloproteinase-2
DR 127497-59-0
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISINSIGHT, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CIN, DDFU, DRUGU, EMBASE, MEDLINE, PHAR, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1191 REFERENCES IN FILE CA (1962 TO DATE)
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1193 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:37164

REFERENCE 2: 138:37069

REFERENCE 3: 138:36820

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REFERENCE 5: 138:22812

REFERENCE 6: 138:22748

REFERENCE 7: 138:22575

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REFERENCE 9: 138:19264

REFERENCE 10: 138:11772

L112 ANSWER 14 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **86102-31-0** REGISTRY
CN Proteinase inhibitor, TIMP (9CI) (CA INDEX NAME)
OTHER NAMES:

CN Metalloproteinase elastase inhibitor
CN TIMP
CN TIMP metalloproteinase inhibitor
CN TIMP proteinase inhibitor
CN Tissue inhibitor of matrix metalloproteinase
CN Tissue inhibitor of metalloproteinase
MF Unspecified
CI MAN
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CIN, PHAR, PROMT, TOXCENTER, USPAT2, USPATFULL

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616 REFERENCES IN FILE CA (1962 TO DATE)
21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
619 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:22918

REFERENCE 2: 138:21791

REFERENCE 3: 138:19488

REFERENCE 4: 137:383081

REFERENCE 5: 137:367257

REFERENCE 6: 137:365343

REFERENCE 7: 137:350835

REFERENCE 8: 137:348213

REFERENCE 9: 137:347243

REFERENCE 10: 137:346861

L112 ANSWER 15 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **79955-99-0** REGISTRY
CN Stromelysin 1 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN E.C. 3.4.24.17
CN Matrix metalloprotease 3
CN Matrix metalloproteinase 3
CN Matrix metalloproteinase MMP-3
CN MMP-3
CN Neutral proteoglycanase
CN Proteoglycanase
CN Stromelysin
CN Transin
DR 107087-03-6, 118368-07-3
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CIN, EMBASE, IPA, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2020 REFERENCES IN FILE CA (1962 TO DATE)
26 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2029 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:37107

REFERENCE 2: 138:37069

REFERENCE 3: 138:36908

REFERENCE 4: 138:36857

REFERENCE 5: 138:35169

REFERENCE 6: 138:34222

REFERENCE 7: 138:33336

REFERENCE 8: 138:32563

REFERENCE 9: 138:29102

REFERENCE 10: 138:23360

L112 ANSWER 16 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **39391-18-9** REGISTRY
CN Synthetase, prostaglandin endoperoxide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Arachidonate cyclooxygenase
CN Arachidonic acid cyclooxygenase
CN Arachidonic cyclooxygenase
CN Cyclooxygenase
CN E.C. 1.14.99.1
CN Fatty acid cyclooxygenase
CN Gene TIS10 proteins
CN Peroxidase, prostaglandin hydroperoxide
CN PG synthetase
CN PGG/H synthase
CN PGG2 peroxidase
CN PGH synthase
CN PGH2 synthase
CN PGH2 synthetase
CN PGI2 cyclooxygenase
CN Prostaglandin cyclooxygenase
CN Prostaglandin endoperoxide G/H synthase
CN Prostaglandin endoperoxide H synthase
CN Prostaglandin endoperoxide synthase
CN Prostaglandin endoperoxide synthetase
CN Prostaglandin G/H synthase
CN Prostaglandin G2 peroxidase
CN Prostaglandin G2/H2 synthase
CN Prostaglandin H synthase
CN Prostaglandin H synthetase
CN Prostaglandin H2 synthase
CN Prostaglandin H2 synthetase
CN Prostaglandin hydroperoxidase
CN Prostaglandin hydroperoxide peroxidase
CN Prostaglandin peroxidase
CN Proteins, gene TIS10
CN TXA2 cyclooxygenase
DR 59763-19-8, 64427-82-3, 69913-02-6
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, EMBASE, NIOSHTIC, PROMT, TOXCENTER, USPAT2, USPATFULL

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7834 REFERENCES IN FILE CA (1962 TO DATE)
79 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

7810 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:44710

REFERENCE 2: 138:36597

REFERENCE 3: 138:36534

REFERENCE 4: 138:33627

REFERENCE 5: 138:33613

REFERENCE 6: 138:33578

REFERENCE 7: 138:33086

REFERENCE 8: 138:20671

REFERENCE 9: 138:19889

REFERENCE 10: 138:19837

L112 ANSWER 17 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **9067-32-7** REGISTRY
CN Hyaluronic acid, sodium salt (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Artz
CN Bio Hyaluro 12
CN FCH 200
CN FCH 248
CN HA-Q
CN HA-Q 1
CN Healon
CN Healon (polysaccharide)
CN Healon GV
CN Hyalart
CN Hyalein
CN Hyalgan
CN Hyladerm
CN Nidelon
CN NRD 101
CN Opegan
CN Orthovisc
CN SI 4402
CN SL 1010
CN SLM 10
CN Sodium hyaluronate
CN SPH
DR 34448-35-6
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyother, Polyother only
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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57 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1381 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:44739

REFERENCE 2: 138:29217

REFERENCE 3: 138:29203

REFERENCE 4: 138:29160

REFERENCE 5: 138:28964

REFERENCE 6: 138:20902

REFERENCE 7: 138:315

REFERENCE 8: 137:389255

REFERENCE 9: 137:389246

REFERENCE 10: 137:389204

L112 ANSWER 18 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **9004-61-9** REGISTRY
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN ACP
CN ACP (polysaccharide)
CN ACP gel
CN Durolane
CN Hyaluronan
CN Hylartil
CN Luronit
CN Mucoitin
CN Sepracoat
CN Synvisc
DR 9039-38-7, 37243-73-5, 29382-75-0
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

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699 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9097 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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REFERENCE 2: 138:44758

REFERENCE 3: 138:44756

REFERENCE 4: 138:44739

REFERENCE 5: 138:44720

REFERENCE 6: 138:44717

REFERENCE 7: 138:44708

REFERENCE 8: 138:44493

REFERENCE 9: 138:40942

REFERENCE 10: 138:40803

L112 ANSWER 19 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **9001-92-7** REGISTRY
CN Proteinase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN .alpha.-N-Benzoyl-DL-arginine-p-nitroanilide hydrolase
CN 537 Acidic protease
CN Actinase
CN Alkalase 2.4L FG
CN Alkalase 2.5L Type DX
CN Alkaline protease-L FG
CN ALP 901
CN AO protease
CN APL 901
CN Aquatinase E
CN Arginine esterase
CN AS 1.398
CN AS 10
CN Azocaseinase
CN BAPAase
CN BAPNAase
CN Benzoyl arginine arylamidase
CN Benzoyl-DL-arginine-p-nitroanilide hydrolase
CN Bioprase SP-4FG
CN Bioprotease A
CN Bioprotease N 100P
CN Carbonyl hydrolase
CN Casein endopeptidase
CN Caseinase
CN Cleanase AP 100-PWC
CN Corolase 7089
CN Corolase L 10
CN DA 10
CN DA 10 (enzyme)
CN Denatyme AP
CN Durazyme 16.0L
CN Endopeptidase
CN Endopeptidase O
CN Endoprotease
CN Endoproteinase
CN Enzylase K 40
CN Enzylon SAL
CN Enzylon SAL 300
CN Enzymes, proteolytic
CN Esteroproteinase
CN Everlase 16L
CN Everlase 16L Type EX
CN Fibrinase
CN Flavorase
CN Flavourzyme 500 MG
CN Fungal Protease P 31000
CN Genencor 4000 S
CN GHPO 525 protease

CN GPR protease
CN Growth-related proteinase
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
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MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PLASPEC*, PROMT, RTECS*, TOXCENTER, TULSA, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

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34479 REFERENCES IN FILE CA (1962 TO DATE)
392 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
34529 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:44498

REFERENCE 2: 138:44492

REFERENCE 3: 138:44457

REFERENCE 4: 138:41033

REFERENCE 5: 138:40618

REFERENCE 6: 138:40581

REFERENCE 7: 138:38547

REFERENCE 8: 138:38520

REFERENCE 9: 138:38474

REFERENCE 10: 138:38472

L112 ANSWER 20 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **9001-12-1** REGISTRY
CN Collagenase (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Aspergillopeptidase C
CN Azocollase
CN Clostridiopeptidase A
CN Clostridiopeptidase I
CN Clostridiopeptidase II
CN Collagen peptidase
CN Collagen protease
CN Collagenase A
CN Collagenase MMP-1
CN E.C. 3.4.24.3
CN E.C. 3.4.24.34
CN E.C. 3.4.24.7
CN E.C. 3.4.4.19
CN E.C. 3.4.99.5
CN Interstitial collagenase

CN Kollaza
CN Liberase
CN Liberase Blendzyme IV
CN Matrix metalloprotase 1
CN Matrix metalloprotease MMP-ABT
CN Matrix metalloproteinase-1
CN Matrix metalloproteinase-18
CN Matrix metalloproteinase-8
CN Metallocollagenase
CN Metalloproteinase-1
CN MMP-1
CN MMP-8
CN Morikraz
CN Nucleolysin
CN Peptidase, clostridio-, A
CN Proteinase, Clostridium histolyticum, A
CN Soycollagestin
DR 37288-86-1, 39433-96-0
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PHAR, PIRA, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
7269 REFERENCES IN FILE CA (1962 TO DATE)
71 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7281 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:44756

REFERENCE 2: 138:44498

REFERENCE 3: 138:38132

REFERENCE 4: 138:37447

REFERENCE 5: 138:37069

REFERENCE 6: 138:37048

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REFERENCE 10: 138:35169

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FILE COVERS 1974 TO 16 Jan 2003 (20030116/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate

substance identification.

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L133 ANSWER 1 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2001370730 EMBASE
TI A critique of the 2000 update of the American College of Rheumatology recommendations for management of hip and knee osteoarthritis [5].
AU Brandt K.D.; Hochberg M.C.
CS Dr. K.D. Brandt, Indiana Univ. School of Medicine, Indianapolis, IN, United States
SO Arthritis and Rheumatism, (2001) 44/10 (2451-2456).
ISSN: 0004-3591 CODEN: ARHEAW
CY United States
DT Journal; Letter
FS 031 Arthritis and Rheumatism
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
CT Medical Descriptors:
*knee osteoarthritis: DM, disease management
*knee osteoarthritis: DT, drug therapy
*coxitis: DM, disease management
*coxitis: DT, drug therapy
medical society
practice guideline
drug contraindication
drug safety
drug efficacy
drug cost
evidence based medicine
expert system
medical literature
peer review
antiinflammatory activity
analgesic activity
drug induced disease: SI, side effect
liver toxicity: SI, side effect
drug overdose
human
clinical trial
letter
priority journal
Drug Descriptors:
hyaluronic acid: DT, drug therapy
hyaluronic acid: AR, intraarticular drug administration
opiate: AE, adverse drug reaction
opiate: DT, drug therapy
opiate: PE, pharmacoeconomics
tramadol: AE, adverse drug reaction
tramadol: DT, drug therapy
tramadol: PE, pharmacoeconomics
paracetamol: AE, adverse drug reaction
paracetamol: CT, clinical trial
paracetamol: CB, drug combination
paracetamol: CM, drug comparison
paracetamol: DO, drug dose
paracetamol: DT, drug therapy
paracetamol: TO, drug toxicity
paracetamol: PE, pharmacoeconomics
analgesic agent: AE, adverse drug reaction
analgesic agent: CT, clinical trial

analgesic agent: CB, drug combination
analgesic agent: CM, drug comparison
analgesic agent: DO, drug dose
analgesic agent: DT, drug therapy
analgesic agent: TO, drug toxicity
analgesic agent: PE, pharmacoeconomics
nonsteroid antiinflammatory agent: AE, adverse drug reaction
nonsteroid antiinflammatory agent: CT, clinical trial
nonsteroid antiinflammatory agent: CM, drug comparison
nonsteroid antiinflammatory agent: DO, drug dose
nonsteroid antiinflammatory agent: DT, drug therapy
phenylbutazone: CM, drug comparison
phenylbutazone: DT, drug therapy
ibuprofen: CT, clinical trial
ibuprofen: CM, drug comparison
ibuprofen: DO, drug dose
ibuprofen: DT, drug therapy
celecoxib: AE, adverse drug reaction
celecoxib: CT, clinical trial
celecoxib: CB, drug combination
celecoxib: DT, drug therapy
rofecoxib: AE, adverse drug reaction
rofecoxib: CT, clinical trial
rofecoxib: DT, drug therapy
acetylsalicylic acid: AE, adverse drug reaction
acetylsalicylic acid: DO, drug dose
acetylsalicylic acid: DT, drug therapy
cyclooxygenase 2 inhibitor: AE, adverse drug reaction
cyclooxygenase 2 inhibitor: CT, clinical trial
cyclooxygenase 2 inhibitor: CB, drug combination
cyclooxygenase 2 inhibitor: DT, drug therapy
cyclooxygenase 1 inhibitor: AE, adverse drug reaction
cyclooxygenase 1 inhibitor: DT, drug therapy
warfarin: AE, adverse drug reaction
warfarin: CB, drug combination
warfarin: DT, drug therapy
corticosteroid: DT, drug therapy
corticosteroid: AR, intraarticular drug administration
glucocorticoid: DT, drug therapy
glucocorticoid: AR, intraarticular drug administration

RN (**hyaluronic acid**) **31799-91-4, 9004-61-9, 9067-32-7**; (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (tramadol) 27203-92-5, 36282-47-0; (paracetamol) 103-90-2; (phenylbutazone) 129-18-0, 50-33-9, 8054-70-4; (ibuprofen) 15687-27-1; (celecoxib) 169590-42-5; (rofecoxib) 162011-90-7, 186912-82-3; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2

L133 ANSWER 2 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2000335279 EMBASE
TI 'Horizons in Rheumatology' 2nd Annual CPD Update Thursday 16th March 2000 Royal College of Pathologists, London.
AU Dawson J.
CS Dr. J. Dawson, Department of Rheumatology, University Hospital Aintree, Longmoor Lane, Liverpool L9 7AL, United Kingdom
SO CPD Rheumatology, (2000) 1/3 (111-112).
ISSN: 1367-8922 CODEN: CPDRFU
CY United Kingdom
DT Journal; Conference Article
FS 007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
031 Arthritis and Rheumatism
038 Adverse Reactions Titles

052 Toxicology
017 Public Health, Social Medicine and Epidemiology
020 Gerontology and Geriatrics
010 Obstetrics and Gynecology
030 PharmacologyGerontology and Geriatrics
LA English
CT Medical Descriptors:
*arthritis: EP, epidemiology
*arthritis: DT, drug therapy
*arthritis: ET, etiology
*arthritis: TH, therapy
*arthritis: DI, diagnosis
*arthritis: DR, drug resistance
human
clinical trial
United Kingdom
Paget bone disease: EP, epidemiology
Paget bone disease: DT, drug therapy
Paget bone disease: DR, drug resistance
osteoarthritis: DI, diagnosis
osteoarthritis: ET, etiology
osteoarthritis: EP, epidemiology
osteoarthritis: DT, drug therapy
osteoarthritis: TH, therapy
aging
juvenile rheumatoid arthritis: DT, drug therapy
risk factor
prevalence
rheumatic disease: TH, therapy
rheumatic disease: DT, drug therapy
conservative treatment
rheumatoid arthritis: DT, drug therapy
rheumatoid arthritis: TH, therapy
pregnancy
maternal disease: SI, side effect
drug safety
immune deficiency: SI, side effect
thrombocytopenia: SI, side effect
coxitis
drug absorption
newborn disease: SI, side effect
conference paper
Drug Descriptors:
***antirheumatic agent: DT, drug therapy**
***antirheumatic agent: CM, drug comparison**
***antirheumatic agent: CB, drug combination**
***antirheumatic agent: TO, drug toxicity**
***antirheumatic agent: AR, intraarticular drug administration**
***antirheumatic agent: PD, pharmacology**
***antirheumatic agent: AE, adverse drug reaction**
***antirheumatic agent: CT, clinical trial**
ascorbic acid: DT, drug therapy
bisphosphonic acid derivative: DT, drug therapy
bisphosphonic acid derivative: PD, pharmacology
alkaline phosphatase: EC, endogenous compound
etidronic acid: DT, drug therapy
calcitonin: DT, drug therapy
nonsteroid antiinflammatory agent: DT, drug therapy
nonsteroid antiinflammatory agent: CM, drug comparison
paracetamol: DT, drug therapy
paracetamol: CM, drug comparison
capsaicin: DT, drug therapy
capsaicin: CT, clinical trial

hyaluronic acid: DT, drug therapy
hyaluronic acid: AR, intraarticular drug administration
hyaluronic acid derivative: DT, drug therapy
hyaluronic acid derivative: AR, intraarticular drug administration
tiludronic acid: DT, drug therapy
methotrexate: DT, drug therapy
methotrexate: CM, drug comparison
methotrexate: TO, drug toxicity
methotrexate: CB, drug combination
methotrexate: PK, pharmacokinetics
tumor necrosis factor alpha antibody: DT, drug therapy
etanercept: DT, drug therapy
etanercept: CM, drug comparison
etanercept: CT, clinical trial
infliximab: DT, drug therapy
infliximab: CM, drug comparison
prednisolone: DT, drug therapy
corticosteroid derivative: AE, adverse drug reaction
hydroxychloroquine: DT, drug therapy
azathioprine: DT, drug therapy
salazosulfapyridine: DT, drug therapy
salazosulfapyridine: AE, adverse drug reaction
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: TO, drug toxicity
leflunomide: DT, drug therapy
leflunomide: CM, drug comparison
leflunomide: CB, drug combination
leflunomide: TO, drug toxicity
RN (ascorbic acid) 134-03-2, 15421-15-5, 50-81-7; (alkaline phosphatase) 9001-78-9; (etidronic acid) 2809-21-4, 3794-83-0, 58449-82-4, 7414-83-7; (calcitonin) 12321-44-7, 21215-62-3, 9007-12-9; (paracetamol) 103-90-2; (capsaicin) 404-86-4; (**hyaluronic acid**) **31799-91-4, 9004-61-9, 9067-32-7**; (tiludronic acid) 96538-83-9; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (etanercept) 185243-69-0, 200013-86-1; (infliximab) 170277-31-3; (prednisolone) 50-24-8; (hydroxychloroquine) 118-42-3, 525-31-5; (azathioprine) 446-86-6; (salazosulfapyridine) 599-79-1; (leflunomide) 75706-12-6
CN Hyalgan
NP synvisc

L133 ANSWER 3 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN **97287685** EMBASE
DN **1997287685**
TI Anti-inflammatory activity of superoxide dismutase conjugated with sodium **hyaluronate**.
AU Sakurai K.; Miyazaki K.; Kodera Y.; Nishimura H.; Shingu M.; Inada Y.
CS Y. Inada, Toin Human Science/Technology Centre, Dept. Materials Science/Technology, Toin University of Yokohama, 1614 Kurogane-cho, Aoba-ku, Yokohama 225, Japan
SO Glycoconjugate Journal, (1997) 14/6 (723-728).
Refs: 32
ISSN: 0282-0080 CODEN: GLJOEW
CY United Kingdom
DT Journal; Article
FS 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
AB Superoxide dismutase (SOD) from bovine erythrocytes was conjugated with sodium **hyaluronate** (HA) with a mean molecular weight of 106 to have greater anti-inflammatory activity in vivo. Amino groups of SOD were

coupled with carboxyl groups in the **hyaluronate** molecule using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide. The HA-SOD conjugate was composed of 1.5 mol of SOD molecule per 1 mol of **hyaluronate** on the average, and retained 70% of the activity of unmodified SOD. The conjugate was essentially non-immunogenic in mice, and exhibited much higher anti-inflammatory activities than HA or SOD in models of inflammatory diseases such as ischemic oedema of the foot-pad in mice, carrageenin-induced pleurisy and adjuvant arthritis in rats.

CT Medical Descriptors:
*adjuvant arthritis
*antiinflammatory activity
*inflammatory disease: DT, drug therapy
animal cell
animal experiment
animal model
article
cattle
controlled study
drug safety
enzyme activity
enzyme binding
enzyme isolation
erythrocyte
immune response
intraarticular drug administration
intraperitoneal drug administration
intravenous drug administration
mouse
nonhuman
priority journal
rat

Drug Descriptors:
*antiinflammatory agent: PD, pharmacology
*antiinflammatory agent: CB, drug combination
*antiinflammatory agent: AN, drug analysis
*antiinflammatory agent: CM, drug comparison
*antiinflammatory agent: DV, drug development
*antiinflammatory agent: DT, drug therapy
*glycoconjugate: PD, pharmacology
*glycoconjugate: DT, drug therapy
*glycoconjugate: AN, drug analysis
***hyaluronic acid: CB, drug combination**
***hyaluronic acid: CM, drug comparison**
***hyaluronic acid: PD, pharmacology**
***superoxide dismutase: CB, drug combination**
***superoxide dismutase: PD, pharmacology**
***superoxide dismutase: DT, drug therapy**
***superoxide dismutase: DO, drug dose**
***superoxide dismutase: CM, drug comparison**
indometacin: CM, drug comparison
indometacin: DT, drug therapy

RN **(hyaluronic acid) 31799-91-4, 9004-61-9, 9067-32-7**; (superoxide dismutase) 37294-21-6, 9016-01-7, 9054-89-1; (indometacin) 53-86-1, 74252-25-8, 7681-54-1

CO Seikagaku (Japan); Sigma (United States)

L133 ANSWER 4 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN **97091232** EMBASE

DN **1997091232**

TI Efficacy of **hyaluronic acid**/nonsteroidal anti-inflammatory drug systems in preventing postsurgical tendon adhesions.

AU Miller J.A.; Ferguson R.L.; Powers D.L.; Burns J.W.; Shalaby S.W.

CS Dr. D.L. Powers, Department of Bioengineering, Clemson University, Clemson, SC 29634-0909, United States
SO Journal of Biomedical Materials Research, (1997) 38/1 (25-33).
Refs: 18
ISSN: 0021-9304 CODEN: JBMRBG
CY United States
DT Journal; Article
FS 027 Biophysics, Bioengineering and Medical Instrumentation
033 Orthopedic Surgery
037 Drug Literature Index
LA English
SL English
AB Tendon adhesion is acknowledged to be a function of both an overwhelming inflammatory response at the surgical site and the loss of physical separation that is normally present between the tendons and the synovial sheath. Adhesions bind the flexor tendons to each other and to surrounding structures, interfering with their normal gliding function. The clinical result of adhesion formation following flexor tendon surgery is poor digital function. This study investigated the effect of intraoperative treatments of high viscosity absorbable gels made of various combinations of **hyaluronic acid** and nonsteroidal anti-inflammatory drugs, on adhesion formation in a leghorn chicken flexor tendon model. Forty-eight mature, white leghorn chickens were used to verify the surgical model and to test five different gel treatments. The gels were formed from: 2% sodium **hyaluronate** in phosphate buffered saline alone or combined with 1 mg/mL tolmetin sodium; 1 mg/mL naproxen sodium; 0.216 g/ml, calcium acetate; or 0.216 g/mL calcium acetate plus 1 mg/mL naproxen sodium. The gels were applied by injecting 0.2 mL of the specified composition into the intrasheath space near the conclusion of the surgical procedure. Gross and histological evaluations were conducted to analyze the efficacy. All of the treatments significant reduced the extent and severity of postsurgical tendon adhesion in this animal model as compared with the control (no gel treatment) ($p < 0.05$). The combination of naproxen sodium and calcium acetate in a high viscosity sodium **hyaluronate** carrier was the most effective composition. The combination of a high viscosity gel and nonsteroidal anti-inflammatory drugs appears to maintain the natural separation between the tendons and their sheaths and decrease the tissue inflammatory response through mediating two of the major stimuli in adhesion formation.

not - conjugate

CT Medical Descriptors:
*adhesion
*drug delivery system
*tendinitis: PC, prevention
*tendinitis: DT, drug therapy
*tendinitis: CO, complication
animal model
antiinflammatory activity
article
chicken
controlled study
drug efficacy
flexor tendon
intramuscular drug administration
intraperitoneal drug administration
intravenous drug administration
nonhuman
postoperative complication
rat
tendon surgery
topical drug administration
Drug Descriptors:
*calcium acetate: PR, pharmaceutics
*calcium acetate: DT, drug therapy

*calcium acetate: CM, drug comparison
*calcium acetate: CB, drug combination
*calcium acetate: AD, drug administration
***hyaluronic acid: AD, drug administration**
***hyaluronic acid: CB, drug combination**
***hyaluronic acid: CM, drug comparison**
***hyaluronic acid: DT, drug therapy**
***hyaluronic acid: PR, pharmaceutics**
***naproxen: CM, drug comparison**
***naproxen: PR, pharmaceutics**
***naproxen: DT, drug therapy**
***naproxen: AD, drug administration**
***naproxen: CB, drug combination**
*nonsteroid antiinflammatory agent: CB, drug combination
*nonsteroid antiinflammatory agent: CM, drug comparison
*nonsteroid antiinflammatory agent: DT, drug therapy
*nonsteroid antiinflammatory agent: PR, pharmaceutics
*nonsteroid antiinflammatory agent: AD, drug administration
*tolmetin: PR, pharmaceutics
*tolmetin: DT, drug therapy
*tolmetin: CM, drug comparison
*tolmetin: CB, drug combination
*tolmetin: AD, drug administration
ibuprofen: DO, drug dose
ibuprofen: AD, drug administration
ibuprofen: DT, drug therapy
RN (calcium acetate) 62-54-4; (**hyaluronic acid**) **31799-91-4, 9004-61-9, 9067-32-7**; (naproxen) 22204-53-1, 26159-34-2; (tolmetin) 26171-23-3, 35711-34-3; (ibuprofen) 15687-27-1
CO Genzyme (United States); Rw johnson (United States); Sigma (United States); Baker (United States)

L133 ANSWER 5 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN **94338422** EMBASE
DN **1994338422**
TI Review and evaluation of 3% diclofenac in **hyaluronan** (D.HA) gel.
AU Russell A.L.; Fraser R.; Willoughby D.; Tomlinson A.; Falk R.E.
CS Academy of Pain Management, 18 Kensington Road,Bramalea, Ont. L6T 4S5, Canada
SO Round Table Series - Royal Society of Medicine, (1994) -/33 (64-71). ISSN: 0268-3091 CODEN: RTSSES
CY United Kingdom
DT Journal; Conference Article
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB 1. D.HA has a unique analgesic action distal from the site of inflammation. 2. Consideration should be given in further trials to extending the age group limit to 75 to cover the cases where topical agents will be most useful. 3. Possible evaluation and double blind study for treatment of thrombophlebitis should be undertaken in an older age group who are at higher risk from oral NSAIDs. 4. Capsaicin should be scientifically evaluated as a test bed for rapid inexpensive evaluation of D.HA, and seems to be ideal for comparison with other NSAIDs. Further work is needed in a university laboratory setting. 5. With the ever-increasing epidemic of myofascial and fibromyalgia, thought should be given to evaluating treatment in this field. In summary, HA in combination with an NSAID will induce local analgesia, and distant analgesia in deeper structures beyond the range of initial diffusion. Can this be explained by an axon reflex? Comments would be appreciated.

not conjugate

CT Medical Descriptors:
*analgesia
antiinflammatory activity
clinical trial
conference paper
drug formulation
drug mechanism
fibromyalgia: DT, drug therapy
human
inflammation: DT, drug therapy
meta analysis
myofascial pain: DT, drug therapy
nerve ending
nerve fiber
nerve stimulation
neuritis: DT, drug therapy
nonhuman
osteoarthritis: DT, drug therapy
pain: DT, drug therapy
patient compliance
soft tissue injury: DT, drug therapy
thermography
thrombophlebitis: DT, drug therapy
tooth extraction
topical drug administration
ulcer: DT, drug therapy
Drug Descriptors:
*diclofenac: CM, drug comparison
*diclofenac: DT, drug therapy
*diclofenac: PR, pharmaceutics
*diclofenac: PD, pharmacology
*diclofenac: CT, clinical trial
antibiotic agent: DT, drug therapy
antibiotic agent: CB, drug combination
capsaicin
hyaluronic acid: CB, drug combination
hyaluronic acid: DT, drug therapy
nonsteroid antiinflammatory agent: CM, drug comparison
piroxicam: CT, clinical trial
piroxicam: CB, drug combination
piroxicam: DT, drug therapy
substance p: EC, endogenous compound
RN (diclofenac) 15307-79-6, 15307-86-5; (capsaicin) 404-86-4; (**hyaluronic acid**) **31799-91-4, 9004-61-9**, **9067-32-7**; (piroxicam) 36322-90-4; (substance p) 33507-63-0
CO Pfizer (Indonesia)

L133 ANSWER 6 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN **94035278** EMBASE
DN **1994035278**
TI The effects of orally administered calcium pentosan polysulfate on inflammation and cartilage degradation produced in rabbit joints by intraarticular injection of a **hyaluronate**-polylysine complex.
AU Smith M.M.; Ghosh P.; Numata Y.; Bansal M.K.
CS Raymond Purves Bone/Joint Res. Lab., Royal North Shore Hospital of Sydney,St. Leonards, NSW 2065, Australia
SO Arthritis and Rheumatism, (1994) 37/1 (125-136).
ISSN: 0004-3591 CODEN: ARHEAW
CY United States
DT Journal; Article
FS 031 Arthritis and Rheumatism
037 Drug Literature Index
LA English

SL English

AB Objective. To determine the antiinflammatory and cartilage-protecting activities of orally administered calcium pentosan polysulfate (CaPPS) in a rabbit model of inflammatory arthritis. Methods. A single intraarticular injection of a preformed polycation complex (PC) of poly-D-lysine and **hyaluronan** was used to induce joint inflammation; saline was injected into the contralateral joint as a control. Animals were killed 1, 4, 7, or 10 days post-PC injection. CaPPS, at 5 mg/kg, 10 mg/kg, or 75 mg/kg, was given every 48 hours commencing 7 days prior to PC injection. Serum interleukin-6 (IL- 6), synovial fluid (SF) prostaglandin E2, cell numbers, and cartilage proteoglycan (PG) content, composition, and biosynthesis were determined for PC- and saline-injected joints. Results. In PC-injected, non-drug-treated animals, serum IL-6 activity, SF leukocyte numbers, and prostaglandin E2 levels were elevated, while cartilage PG content and biosynthesis were reduced. CaPPS at 10 mg/kg, but not at 5 mg/kg, decreased serum IL-6 levels but maintained cartilage PG concentration and biosynthesis. However, SF leukocyte counts and prostaglandin E2 levels (except on day 1) were not reduced. Conclusion. The ability of CaPPS to attenuate serum IL-6 levels and preserve cartilage PGs in inflamed rabbit joints suggests that this substance could be of value as an effective orally administered chondroprotective, antiarthritic drug.

CT Medical Descriptors:
*cartilage degeneration
*osteoarthritis
*rheumatoid arthritis
animal experiment
animal model
article
controlled study
dose response
drug efficacy
drug mixture
nonhuman
priority journal
protein content
rabbit
synovial fluid
Drug Descriptors:
*calcium: CB, drug combination
*calcium: DO, drug dose .
*calcium: PD, pharmacology
***hyaluronic acid: CB, drug combination**
***hyaluronic acid: PD, pharmacology**
***pentosan polysulfate: CB, drug combination**
***pentosan polysulfate: DO, drug dose**
***pentosan polysulfate: PD, pharmacology**
*polylysine: CB, drug combination
*polylysine: PD, pharmacology
interleukin 6: EC, endogenous compound
prostaglandin e2: EC, endogenous compound
proteoglycan: EC, endogenous compound

RN (calcium) 7440-70-2; (**hyaluronic acid**) **31799-91-4, 9004-61-9, 9067-32-7**; (pentosan polysulfate) 116001-96-8, 37300-21-3, 37319-17-8; (polylysine) 25104-18-1, 25988-63-0, 33960-24-6, 38000-06-5, 73565-56-7; (prostaglandin e2) 363-24-6

L133 ANSWER 7 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN **93196741** EMBASE

DN **1993196741**

TI Animal models of early osteoarthritis: Their use for the evaluation of potent chondroprotective agents.

AU Ghosh P.; Armstrong S.; Read R.; Numata Y.; Smith S.; McNair P.; Marshall R.
CS Raymond Purves Research Laboratories, University of Sydney, Royal North Shore Hospital of Sydney,St Leonards, NSW 2065, Australia
SO Agents and Actions, (1993) 39/SUPPL. (195-206).
ISSN: 0065-4299 CODEN: AGACBH
CY Switzerland
DT Journal; Conference Article
FS 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
AB Medial meniscectomy was undertaken in adult merino sheep and after 16 weeks exercise each group was administered five weekly intra-articular injections of saline, pentosan polysulphate (PPS), **hyaluronic acid** (HA) or a combination of PPS + HA. Gait analysis and x-rays were undertaken before and after drug treatment. At sacrifice (26 weeks), joints were examined for gross pathological and histochemical changes. Only the PPS-treated group showed an improvement in gait, with low radiological and histology scores. The HA-treated group showed similar but less significant changes to these parameters.
CT Medical Descriptors:
*drug screening
*osteoarthritis: PC, prevention
animal experiment
animal model
conference paper
controlled study
exercise
gait
histochemistry
meniscectomy
nonhuman
pathology
priority journal
sheep
X ray
Drug Descriptors:
*protective agent: CB, drug combination
*protective agent: CM, drug comparison
hyaluronic acid: CB, drug combination
hyaluronic acid: CM, drug comparison
pentosan polysulfate: CB, drug combination
pentosan polysulfate: CM, drug comparison
RN (**hyaluronic acid**) **31799-91-4, 9004-61-9, 9067-32-7**; (pentosan polysulfate) 116001-96-8, 37300-21-3, 37319-17-8
CN (1) Artz; Cartrophen
CO (1) Seikayaku (Japan)

L133 ANSWER 8 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN **91244798** EMBASE
DN **1991244798**
TI [Comparison between the bioavailability of two topical formulas of piroxicam in the presence and absence of thiomucase].
BIODISPONIBILIDADE COMPARADA DE DUAS FORMULACOES DE APLICACAO CUTANEA DE PRIOXICAM NA PRESENCA E AUSENCIA DE TIOMUCASE.
AU Maya M.; Morais J.; Ruas da Silva J.
CS Centro de Metabolismos e Genetica, Universidade de Lisboa, Lisboa, Portugal
SO Revista Portuguesa de Farmacia, (1991) 41/2 (33-41).
CODEN: RPTFAU

CY Portugal
DT Journal; Article
FS 037 Drug Literature Index
LA Portuguese
SL English
CT Medical Descriptors:
*drug absorption
*drug bioavailability
*drug formulation
*drug penetration
*skin permeability
adult
article
drug blood level
drug determination
drug structure
high performance liquid chromatography
human
human experiment
male
normal human
topical drug administration
Drug Descriptors:
*enzyme
***piroxicam: PK, pharmacokinetics**
***piroxicam: CB, drug combination**
***piroxicam: AN, drug analysis**
***hyaluronidase: CB, drug combination**
RN (piroxicam) 36322-90-4; (**hyaluronidase**) **9001-54-1**, 9055-18-9

```
=> e antirheumatic agent+all/ct
E1            0   BT3   Chemicals and drugs/CT
E2            1    BT2   analgesic, antiinflammatory, antirheumatic and
                         antigout agents/CT
E3        12170     BT1   antiinflammatory agent/CT
E4         3424      -->   antirheumatic agent/CT
E5       105421      MN    D14.30.40./CT
                      HNTE  Creation date  01 JUL 19: 79
E6            0       UF    antiarthritic agent/CT
E7            0       UF    antirheumatic/CT
E8            0       UF    antirheumatic agents/CT
E9            0       UF    antirheumatic agents, gold/CT
E10           0       UF    antirheumatic drug/CT
E11          28       NXT   (10 methoxy 4h benzo(4,5)cyclohepta(1,2 b)thiophen
                            4 ylidene)acetic acid/CT
E12           6       NXT   2 (4 chlorophenyl) 4,5 diphenyl 2 imidazoline/CT
E13          21       NXT   3 (3,5 di tert butyl 4 hydroxybenzylidene) 1
                            methoxy 2 pyrrolidinone/CT
E14           2       NXT   3 (4 methylbenzoyl) 2 (methylthiomethyl)propionic
                            acid/CT
E15          18       NXT   3 aurothio 2 hydroxy 1 propanesulfonate calcium/CT
E16          29       NXT   3 formamido 7 methanesulfonamido 6
                            phenoxychromone/CT
E17           9       NXT   3,7 dimethyl 9 (2 nonyloxy 6
                            (trifluoromethyl)phenyl) 2,4,6,8 nonatetraenoic
                            acid/CT
E18           4       NXT   3,7 dimethyl 9 (2 nonyloxyphenyl) 2,4,6,8
                            nonatetraenoic acid/CT
E19          12       NXT   4 (1 (2 fluoro 4 biphenylyl)ethyl) 2
                            methylaminothiazole/CT
E20           7       NXT   4 (3,4 dimethoxyphenyl) 6,7 dimethoxy 2 (1,2,4
```

			triazol 1 ylmethyl) 3 quinolinecarboxylic acid ethyl ester/CT
E21	31	NXT	4 (3,5 di tert butyl 4 hydroxyphenyl) 2 methyl 1,2 oxazin 3 one/CT
E22	35	NXT	acetylsalicylate copper/CT
E23	183	NXT	acetylsalicylic acid calcium/CT
E24	61	NXT	actarit/CT
E25	37	NXT	adalimumab/CT
E26	233	NXT	allochrysine/CT
E27	57	NXT	amiprilose/CT
E28	68	NXT	anacin/CT
E29	140	NXT	arthrotec/CT
E30	2	NXT	atiprimod/CT
E31	1619	NXT	auranofin/CT
E32	1030	NXT	aurothioglucose/CT
E33	2363	NXT	aurothiomalate/CT
E34	961	NXT	azapropazone/CT
E35	31392	NXT	azathioprine/CT
E36	721	NXT	benzydamine/CT
E37	270	NXT	bucillamine/CT
E38	178	NXT	bumadizone/CT
E39	34	NXT	butibufen/CT
E40	1825	NXT	celecoxib/CT
E41	14261	NXT	chloroquine/CT
E42	95	NXT	chondroprotective agent/CT
E43	113	NXT	cinchophen/CT
E44	77	NXT	clobuzarit/CT
E45	249	NXT	clometacin/CT
E46	727	NXT	colloidal gold/CT
E47	22	NXT	cph 82/CT
E48	153	NXT	deethylchloroquine/CT
E49	52	NXT	dexketoprofen/CT
E50	147	NXT	diacetylrhein/CT
E51	30	NXT	efalizumab/CT
E52	5	NXT	endolac/CT
E53	12	NXT	esonarimod/CT
E54	1016	NXT	etanercept/CT
E55	207	NXT	etofenamate/CT
E56	2195	NXT	formic acid/CT
E57	49	NXT	galactosaminoglucuronoglycan sulfate/CT
E58	205	NXT	glucosamine sulfate/CT
E59	45	NXT	glucuronylglucosaminoglycan/CT
E60	190	NXT	glycosaminoglycan peptide/CT
E61	813	NXT	glycosaminoglycan polysulfate/CT
E62	4259	NXT	hydroxychloroquine/CT
E63	133	NXT	hydroxychloroquine sulfate/CT
E64	1427	NXT	infliximab/CT
E65	279	NXT	isoxicam/CT
E66	93	NXT	keratinate gold/CT
E67	5119	NXT	ketoprofen/CT
E68	51	NXT	ketoprofen lysine/CT
E69	1153	NXT	leflunomide/CT
E70	72	NXT	lenercept/CT
E71	6	NXT	licofelone/CT
E72	165	NXT	lobenzarit/CT
E73	56	NXT	lonazolac calcium/CT
E74	124	NXT	lornoxicam/CT
E75	2	NXT	lumiracoxib/CT
E76	70	NXT	magnesium salicylate/CT
E77	1046	NXT	melittin/CT
E78	189	NXT	n acetylpenicillamine/CT
E79	969	NXT	nabumetone/CT
E80	10212	NXT	naproxen/CT

E81	8	NXT	neurofenac/CT
E82	1213	NXT	niflumic acid/CT
E83	79	NXT	om 89/CT
E84	688	NXT	osmium tetraoxide/CT
E85	86	NXT	oxaceprol/CT
E86	11027	NXT	penicillamine/CT
E87	907	NXT	pentosan polysulfate/CT
E88	54	NXT	piascledine/CT
E89	5910	NXT	piroxicam/CT
E90	103	NXT	piroxicam beta cyclodextrin/CT
E91	5	NXT	pralnacasan/CT
E92	14	NXT	prinomide/CT
E93	10	NXT	prinomide triethanolamine/CT
E94	241	NXT	rhein/CT
E95	16	NXT	rheumajecta/CT
E96	98	NXT	rimexolone/CT
E97	1395	NXT	rofecoxib/CT
E98	26	NXT	s adenosylmethionine tosylate sulfate/CT
E99	248	NXT	sodium aurothiosulfate/CT
E100	3538	NXT	sulindac/CT
E101	190	NXT	sulindac sulfide/CT
E102	16299	NXT	superoxide dismutase/CT
E103	272	NXT	tenidap/CT
E104	59	NXT	tepoxalin/CT
E105	44	NXT	teriflunomide/CT
E106	48	NXT	thurfyl nicotinate/CT
E107	966	NXT	tiaprofenic acid/CT
E108	34	NXT	tilomisole/CT
E109	55	NXT	timegadine/CT
E110	416	NXT	tolfenamic acid/CT
E111	27	NXT	tropesin/CT
E112	39	NXT	vasolastine/CT
E113	3	NXT	zinc chelated pentosan polysulfate/CT
E114	3	NXT	zinc glycerolate/CT

********* END***

=> fil wpix
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=> d all abeq tech abex tot

L169 ANSWER 1 OF 6 WPIX (C) 2003 THOMSON DERWENT
AN **2002-537443** [57] WPIX
DNC **C2002-152395**
TI New hydroxamic acid compounds containing **hyaluronic acid** are **matrix metalloproteinase inhibitors** for treating arthritis.
DC B02 B05
IN IKEYA, H; MORIKAWA, T; **OKAMACHI, A**; TAKAHASHI, K; **TAMURA, T**
PA (CHUS) CHUGAI SEIYAKU KK; (ELED) DENKI KAGAKU KOGYO KK
CYC 99
PI WO 2002044218 A1 20020606 (200257)* JA 39p C08B037-08 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002018512 A 20020611 (200264) C08B037-08 <--
ADT WO 2002044218 A1 WO 2001-JP10493 20011130; AU 2002018512 A AU 2002-18512 20011130
FDT AU 2002018512 A Based on WO 200244218
PRAI JP 2000-363993 20001130
IC ICM **C08B037-08**
ICS **A61K031-728**; A61P019-02; A61P029-00
AB WO 200244218 A UPAB: 20021031
NOVELTY - Hydroxamic derivatives (I) are new.
DETAILED DESCRIPTION - Hydroxamic derivatives of formula (I) are new.
R1 = H, OH, 1-8C alkyl, 1-8C alkoxy or 2-8C alkenyl;
R2, R3 = 1-8C alkyl (optionally substituted by 3-10C cycloalkyl or optionally substituted 6-14C aryl); or
R1+R3 = ring.
R4 = H or 1-4C alkyl;
R5 = R7-R8-R9;
R7 = 1-8C alkylene;
R8 = O or CH2 or NH both optionally substituted by 1-4C alkyl;
R9 = 1-10C alkylene optionally interrupted by O; and
R6 = H or 1-4C alkyl.
ACTIVITY - Antiarthritic; **Antirheumatic**; Osteopathic.
In an in vitro collagen induced arthritis model using rabbit femurs a compound of formula (Ia) had an IC50 value of 100 micro g/ml.
MECHANISM OF ACTION - **Matrix-Metalloproteinase-Inhibitor**
USE - As **matrix metalloproteinase inhibitors** for treating and preventing arthritic diseases such as **rheumatoid** arthritis and osteoarthritis.
Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: B04-C02D; **B14-C06**; B14-C09; B14-D07C
TECH UPTX: 20020906
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) are prepared by reacting an amino compound of formula (IX) with N-hydroxy-5-norbornene-2,3-dicarboximide and **hyaluronic acid**.

R14 = amino protecting group.

ABEX

SPECIFIC COMPOUNDS - Five compounds (I) are specifically claimed e.g. (Ia).
HA = **hyaluronic acid** its derivative or salt attached via a hydroxyl group.

ADMINISTRATION - Dosage is 0.01-100 (preferably 0.1-10) mg/kg/day by injection.

EXAMPLE - Pyridine (1.2 ml), 1N hydrochloric acid (12 ml) in water (46.8 ml), N-hydroxy-5-norbornene-2,3-dicarboximide (1.068 g) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.152 g) were added to sodium **hyaluronate** (600 mg; weight average molecular weight = 2200000) in water (60 ml). The mixture was stirred overnight at 40 degrees C and worked up. 0.1N Sodium hydroxide (20 ml) was added to an aqueous solution of N'-(13-amino-4,7,10-trioxatridecanyl)-N-(3S-hydroxy-4-(N-(1-methylethoxy)amino)-2R-isobutylsuccinyl)-L-t-leucinamide (25 mM; 20 ml) and the above **hyaluronic acid** product and the mixture was reacted at 4 degrees C for 22 hours. Work-up gave a compound of formula (Ia).

L169 ANSWER 2 OF 6 WPIX (C) 2003 THOMSON DERWENT
AN **2002-257275** [30] WPIX
DNC **C2002-076529**
TI New cationic **matrix metalloprotease inhibitors** for treating arthritis.
DC B05
IN HAYASHI, Y; NAKAMURA, T; **OKAMACHI, A; TAMURA, T**
PA (CHUS) CHUGAI SEIYAKU KK
CYC 96
PI WO 2002006227 A1 20020124 (200230)* JA 90p C07D209-20
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001071068 A 20020130 (200236) C07D209-20
ADT WO 2002006227 A1 WO 2001-JP6172 20010717; AU 2001071068 A AU 2001-71068 20010717
FDT AU 2001071068 A Based on WO 200206227
PRAI JP 2000-398635 20001227; JP 2000-216790 20000718
IC ICM C07D209-20
ICS A61K031-405; A61K038-05; A61K038-06; A61K038-07; A61P019-02; A61P029-00; A61P043-00
AB WO 200206227 A UPAB: 20020513
NOVELTY - Cationic **matrix metalloprotease inhibitors** and theirs salts are new.
ACTIVITY - Antiarthritic; Osteopathic; **Antirheumatic.**
MECHANISM OF ACTION - **Matrix-Metallo-Proteinase-Inhibitor**
USE - As **matrix metalloprotease inhibitors** for treating and preventing arthritis including osteoarthritis and **rheumatoid** arthritis.
ADVANTAGE - Have improved retention at affected part of body thus have improved activity and reduced side effects.
Dwg.0/10
FS CPI
FA AB; DCN
MC CPI: B06-H; B07-H; B10-A09B; B10-A10; B10-A17; B10-A18; B14-C09A; B14-C09B
TECH UPTX: 20020513
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - More Specifically: Cationic

matrix metalloprotease inhibitor comprises a hydroxamic group (preferably of formula (I) optionally attached via a spacer R7R8R9R10) and is especially a **hyaluronic acid** or its derivative.
R1 = H, OH, A, OA, 2-8C alkenyl, (CH2)mNR5R6 or CH2SOnB;
A = 1-8C alkyl;
R5, R6 = H, A (optionally substituted by Cyc) or acyl; or
NR5R6 = ring;
m = 0-4;
B = H, Cyc or A (optionally substituted by Cyc);
Cyc = cycloalkyl, aryl or heterocyclyl);
n = 0-2;
R2, R3 = A (optionally substituted by Cyc);
R4 = H or 1-4C alkyl; or
R1+R3 = ring;
R7 = 1-8C alkylene;
R8 = CH2 (optionally substituted by 1-4C alkyl), O or NH;
R9 = 1-10C alkylene optionally interrupted by 1-3 O;
R10 = O, S or NR11;
R11 = H or 1-4C alkyl.
Preparation: Compounds are prepared by introducing cationic groups into the **matrix metalloprotease inhibitors**.

ABEX

ADMINISTRATION - Dosage is 0.01-100 (preferably 0.1-10) mg/kg/day by injection. Administration may also be orally, systemically or topically.

EXAMPLE - Nalpha,approximatelyo1,approximatelyo2-tris(benzyloxycarbonyl)-D-arginine (0.86 g) then 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloric acid salt were added to N-(4-(N-benzyloxyamino)-2-isobutylsuccinyl)-L-tryptophan-N-(13-amino)-4,7,10-trioxa-tridecanyl) amide (1.0 g) in dichloromethane (10 ml) and the mixture was stirred fo 16 hours at room temperature. Work-up including silica gel chromatography (chlorofrom/methanol) gave 0.62 g (33.7%) of product. The product(0.48 g) was deprotected using palladium charcoal and hydrogen to give 0.25 g (86.2%)of N-(4-(N-hydroxyamino)-2-isobutylsuccinyl)-L-tryptophan-N-(13-N-D-arginylamino-4,7,10-trioxa-tridecanyl)amide.

L169 ANSWER 3 OF 6 WPIX (C) 2003 THOMSON DERWENT
AN **2001-586154** [66] WPIX
DNC **C2001-173702**
TI New composition for **matrix metalloproteinase inhibitor** comprises **hyaluronic acid** polysulfate or dermatan polysulfate.
DC B04
PA (MARU-N) MARUHO KK
CYC 1
PI JP 2001163789 A 20010619 (200166)* 6p A61K031-728 <--
ADT JP 2001163789 A JP 1999-353028 19991213
PRAI JP 1999-353028 19991213
IC ICM **A61K031-728**
ICS A61K031-737; A61P017-00; A61P027-02; A61P043-00
ICA C08B037-00; C08B037-08
AB JP2001163789 A UPAB: 20011113
NOVELTY - New composition for **matrix metalloproteinase** (MMP) **inhibitor** comprises at least one substance selected from **hyaluronic acid** polysulfate, dermatan polysulfate or their salts.
ACTIVITY - Antiinflammatory; dermatological; cytostatic; ophthalmological; antiulcer.
No biological data given.
MECHANISM OF ACTION - MMP (**matrix metalloproteinase**) **inhibitor**.
To fluorescence labeled substrate solution was added MMP-3 derived

from human ulcerative cells to carry our enzyme reaction, and fluorescent intensity (520 nm) of the substrate decomposed product (erected wavelength:495 nm) was measured. **Hyaluronic acid** polysulfate and dermatan polysulfate were added to the reaction solution, adjusting at 10-7 M respectively, and MMP-3 **inhibitory** activity of each sample was evaluated. The results showed that **hyaluronic acid** polysulfate (10-7 M concentration) **inhibited** MMP-3 activity by 20 % and dermatan polysulfate did by 50 %.

USE - The composition is for the prevention or treatment of various diseases accompanied by decomposition of extracellular **matrix**. Various diseases are dermal disorder such as injury; or ulcerative, bullosus, granulomatous and lichenoid dermatitis; or eye disorder such as corneal ulcer and retinopathy. Injury or ulcerative dermatitis is wound, burn, chronic ulcer, decubital ulcer, pyogenic granuloma or dermal disorder caused by sunshine. Bullosus, granulomatous or lichenoid dermal disorder is pemphigus, porphyria cutanea tarda, epidermolysis bullosa dystrophica, epidermolysis bullosa hereditaria simplex, dermatitis herpetiformis, erysipelas, pompholyx, granuloma annulare, necrobiosis lipoidica diabeticorum or lichen planus (all claimed).

The composition is used as MMP **inhibitor**, and effective for the prevention and treatment of inflammatory disorder, dermal disorder, cancer, circulatory disorder, eye disorder or nerve inflammatory disorder.

ADVANTAGE - The compound is safe and has a different structure from the conventional MMP **inhibitors**.

Dwg.0/1

FS CPI
FA AB; DCN
MC CPI: B04-C02E; B04-C02E1; B14-C03; B14-D07C; B14-E08; B14-F02; B14-H01; B14-J01; B14-N03; B14-N17; B14-N17A; B14-N17B; B14-N17C

L169 ANSWER 4 OF 6 WPIX (C) 2003 THOMSON DERWENT

AN **1999-542703** [46] WPIX
DNN **N1999-402500** DNC **C1999-158533**
TI Wound dressing comprising carrier with covalently bonded substances for removal of factors present in wound exudate which disturb healing.
DC A96 B04 B07 D16 D22 P32 P34
IN EICHNER, W; ETTNER, N; MEYER-INGOLD, W; SCHINK, M; MEYEROLD, W
PA (BEIE) BEIERSDORF AG; (EICH-I) EICHNER W; (ETTN-I) ETTNER N; (MEYE-I) MEYEROLD W; (SCHI-I) SCHINK M
CYC 27
PI EP 945144 A2 19990929 (199946)* DE 21p A61L015-42
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
DE 19813663 A1 19991007 (199947) A61L015-42
AU 9921334 A 19991007 (199954) A61L015-38
US 6156334 A 20001205 (200066) A61F013-00
US 2002018802 A1 20020214 (200214) A61K039-395
US 2002197257 A1 20021226 (200304) A61K039-395
ADT EP 945144 A2 EP 1999-250092 19990326; DE 19813663 A1 DE 1998-19813663 19980327; AU 9921334 A AU 1999-21334 19990322; US 6156334 A US 1999-276687 19990326; US 2002018802 A1 Div ex US 1999-276687 19990326, Cont of US 2000-675253 20000929, US 2001-932926 20010821; US 2002197257 A1 Div ex US 1999-276687 19990326, Cont of US 2000-675253 20000929, Cont of US 2001-932926 20010821, US 2002-150015 20020520
FDT US 2002018802 A1 Div ex US 6156334; US 2002197257 A1 Div ex US 6156334
PRAI DE 1998-19813663 19980327
IC ICM A61F013-00; A61K039-395; A61L015-38; A61L015-42
ICS A01N025-00; A61K009-14; A61K009-70; A61K038-43; A61K047-30; A61L015-40; A61L015-44
AB EP 945144 A UPAB: 19991207
NOVELTY - A carrier-based wound dressing supports covalently bonded substances which interact with and remove factors present in the wound exudate which prevent or slow wound healing.

DETAILED DESCRIPTION - A wound dressing comprises a carrier and substances which are covalently bonded to the carrier and which interact by binding, complexing, chelating or chemically reacting with factors comprising suspended cells, cell fragments and dissolved components which are present in the wound exudate and which prevent wound healing.

An INDEPENDENT CLAIM is also included for the preparation of the wound dressing.

USE - Especially for the treatment of chronic, i.e. severe or non-healing, wounds.

ADVANTAGE - The wound dressing is more effective when used on chronic wounds than conventional dressings, e.g. moist dressings (see Nature 1962; 193:293 and Wound Rep. Reg. 1994; 2:202) and Sorbact (RTM: stearic acid coupled to a hydrophobised cellulose dressing).

Dwg.0/4

FS CPI GMPI

FA AB; DCN

MC CPI: A12-V03A; B04-B04C; B04-C02A; B04-C02D; B04-C02E; B04-C02F; B04-C03B; B04-C03D; B04-H06; B04-L01; B04-N04; B07-D04C; B10-A18; B14-D07C; B14-N17B; D05-A01A1; D05-A01A2; D05-A01B1; D05-H10; D09-C04B

TECH UPTX: 19991110

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preparation: The wound dressing is prepared by reacting the substances which interact with the problem factors present in the exudate with the carrier material. Preferred Dressing: The dressing is a bandage, compress, wadding, plaster, foil, film, hydrocolloid bandage or gel. It can contain substances which promote wound healing, especially growth factors, and can also be water absorbent. Preferred Carrier: The carrier is a natural or synthetic polymer, especially cellulose or a cellulose derivative or an alginate, **hyaluronic acid**, chitin, chitosan, polysaccharide, polyamide, polyester, polyolefin, polyacrylate, polyvinyl alcohol, polyurethane or silicone, alone or as a mixture or copolymer. Preferred Covalently Bonded Substances: These substances are especially antigens, chelators, enzyme **inhibitors**, enzymes, enzyme mimetics, peptides and other proteins, which can interact with especially antigens, radicals, ions, proteins, peptides, lipids and free fatty acids. The substance can be a chelator, e.g. desferrioxamine, diethylenetriaminepentaacetic acid, N,N'-bis-(o-hydroxybenzyl)-ethylenediamine-N,N'-diacetic acid, 1,2-dimethyl-3-hydroxypyrid-4-one or 1,2-dimethyl-3-hydroxy-3-hydroxypyridin-4-one, for interaction with ions, especially desferrioxamine for interaction with Fe(III) ions. Alternatively, the substance can be a radical scavenger, e.g. superoxide dismutase, catalase, glutathione peroxidase, myeloperoxidase and/or an enzyme mimic for interaction with reactive oxygen atoms. Further, when the problem factor in the exudate is a **protease**, the covalently bonded substance can be a **protease inhibitor**, especially antipain, leupeptin, cystain, diisopropyl fluorophosphate , 4-(2-aminoethyl)-phenylsulphonyl fluoride, phenylmethanesulphonyl fluoride, a natural proteinogenic **matrix metalloproteinase inhibitor**, aprotinin, alpha-2-antiplasmin, alpha-2-macroglobulin, alpha-1-antichymotripsin, soya bean trypsin **inhibitor** or alpha-1-**protease inhibitor**.

ABEX

EXAMPLE - A cotton bandage (5 g) was boiled in bicarbonate buffer (100 mM) for 0.5 hour, rinsed (H_2O; 2 l), air-dried, dehydrated (acetone), vacuum dried, activated with 1,1'-carbonyldiimidazole (5 g; freshly prepared in acetone (500 ml)) for 1 hour under reflux and then washed (acetone). Desferrioxamine mesylate (3.28 g) was dissolved in bicarbonate buffer (500 ml; 100 mM; pH 8.5) and pumped in countercurrent for 18 hours through a column containing the activated bandage. The resulting cellulose/desferrioxamine bandage is washed (bicarbonate buffer) an air-dried. In a test for iron uptake, the cellulose/desferrioxamine bandage obtained took up 38 mumol/g (32%) of the iron provided, while an

untreated cellulose bandage and a non-activated cellulose desferrioxamine bandage took up only 4 mumol/g (3%).

L169 ANSWER 5 OF 6 WPIX (C) 2003 THOMSON DERWENT
AN **1996-010700** [01] WPIX
DNN **N1996-009247** DNC **C1996-003355**
TI Medical polymer gel for wound dressing etc. - comprising water-swellable gel, spacer, enzyme-hydrolysable unit and active component.
DC A96 B07 D22 P34
IN KINOSHITA, H; TANIHARA, M
PA (KURS) KURARAY CO LTD
CYC 18
PI WO 9531223 A1 19951123 (199601)* EN 62p A61L015-01
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: US
JP 08024325 A 19960130 (199614) 21p A61L025-00
EP 712635 A1 19960522 (199625) EN 29p A61L015-00
R: DE FR GB IT
US 5658592 A 19970819 (199739) 21p A61K009-10
US 5770229 A 19980623 (199832) A61K009-10
JP 2000070356 A 20000307 (200023) 20p A61L024-00
JP 3107726 B2 20001113 (200060) 21p C08J003-075
ADT WO 9531223 A1 WO 1995-JP873 19950508; JP 08024325 A JP 1995-125838 19950425; EP 712635 A1 EP 1995-917511 19950508, WO 1995-JP873 19950508; US 5658592 A WO 1995-JP873 19950508, US 1996-571976 19960116; US 5770229 A Div ex WO 1995-JP873 19950508, Div ex US 1996-571976 19960116, US 1997-826097 19970324; JP 2000070356 A Div ex JP 1995-125838 19950425, JP 1999-269359 19950425; JP 3107726 B2 JP 1995-125838 19950425
FDT EP 712635 A1 Based on WO 9531223; US 5658592 A Based on WO 9531223; US 5770229 A Div ex US 5658592; JP 3107726 B2 Previous Publ. JP 08024325
PRAI JP 1994-124158 19940513
REP DE 2627125; DE 3614095; EP 185070; EP 247362; JP 51149883; JP 565663; JP 60130601; JP 61502310; JP 62254763; US 4152170; US 4226232; US 4716154
IC ICM A61K009-10; A61L015-00; A61L015-01; A61L024-00; A61L025-00; C08J003-075
ICS A61K009-00; A61K047-30; A61K047-36; A61K047-48; A61L015-16; A61L027-00; C08B037-04; **C08B037-08**
AB WO 9531223 A UPAB: 19960108
A polymer gel for pharmaceutical use comprises a water-swellable polymer gel with a drug bonded to it of formula A-X-Y-D (I). A = water-swellable polymer gel; X = spacer; Y = a degradable gp. with a main chain that can be broken by an enzyme; D = drug. Also claimed is a water-swellable polymer gel (A') comprising a polysaccharide contg. carboxy gps., crosslinked by a cpd. of formula R1-NH-(CH2)n-NH-R2 (II) or its salt. R1, R2 = H or COCH(NH2)-(CH2)4-NH2; n = 2-18.
USE - The gel is used to cover wounds including cuts, burns and surgical wounds; as a protective cover (pseudo skin) for bed sores and ulcers; as an adhesive for living tissue; to reinforce bone; and as drug-release material. (A') is used as A in (I).
ADVANTAGE - The gel A' is heat-resistant, transparent and biocompatible, with high safety. (I) promotes wound healing and may contain growth factors, **metalloproteinase inhibitors**, antibiotics, steroids, etc.
Dwg.0/3
FS CPI GMPI
FA AB; DCN
MC CPI: A03-A00A; A08-D03; A12-S; A12-V01; A12-V03A; B04-C02D; B04-C02E; B12-M03; B14-N01; B14-N17; D09-C04B
ABEQ US 5658592 A UPAB: 19970926
A water swelling polymer gel produced by covalently crosslinking a polysaccharide having a carboxyl group within the molecule with a crosslinking reagent represented by the following general formula R1HN-(CH2)n-NHR2 (II) (wherein n is 2-18; and R1 and R2 independently

represent hydrogen atom or the group represented by -COCH(NH2)-(CH2)4-NH2) or a salt thereof, in which the crosslinking reagent is present in an amount 1-50 mole % with respect to the carboxyl group of the polysaccharide.
Dwg.0/3

L169 ANSWER 6 OF 6 WPIX (C) 2003 THOMSON DERWENT
AN **1994-036539** [05] WPIX
DNC **C1994-016777**
TI Compsns. for treating **rheumatoid** arthritis - contg. lipid-bound glycosaminoglycan..
DC B04
IN AOKI, S; IWASAKI, S; KIMATA, K; SUGIURA, N; SUZUKI, S
PA (SEGK) SEIKAGAKU KOGYO CO LTD
CYC 18
PI EP 581282 A1 19940202 (199405)* EN 25p A61K031-735
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
AU 9344314 A 19940203 (199411) A61K031-725
JP 06072893 A 19940315 (199415) 22p A61K037-20
CA 2101482 A 19940131 (199416) A61K031-725
US 5470578 A 19951128 (199602) 18p A61K037-22
AU 668963 B 19960523 (199628) A61K031-725
EP 581282 B1 19990512 (199923) EN A61K031-735
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69324859 E 19990617 (199930) A61K031-735
ADT EP 581282 A1 EP 1993-112169 19930729; AU 9344314 A AU 1993-44314 19930729; JP 06072893 A JP 1992-203558 19920730; CA 2101482 A CA 1993-2101482 19930728; US 5470578 A US 1993-98936 19930729; AU 668963 B AU 1993-44314 19930729; EP 581282 B1 EP 1993-112169 19930729; DE 69324859 E DE 1993-624859 19930729, EP 1993-112169 19930729
FDT AU 668963 B Previous Publ. AU 9344314; DE 69324859 E Based on EP 581282
PRAI JP 1992-203558 19920730
REP 4.Jnl.Ref; EP 466966; EP 493622
IC ICM A61K031-725; A61K031-735; A61K037-20; A61K037-22
ICS A61K009-48; A61K031-715; C07H005-06
AB EP 581282 A UPAB: 19940315
Antirheumatic compsns. comprise a lipid-bound glycosaminoglycan (I) opt. in salt form, and a carrier. (I) are described in JA4-80201 and 4-80202.
(I) comprises chondroitin sulphate, dermatan sulphate or **hyaluronic acid** bound to a glycerolipid, pref. a glycerophospholipid or glyceride, esp. phosphatidyl ethanolamine (PE) or phosphatidyl serine. (I) is prepd. by oxidising the reducing terminal of the glycosaminoglycan, lactonising the prod. and reacting the lactone with an NH2-contg. lipid to form an amide bond. Binding may also be via an aminoalkyl or ester bond. The compsns. are formulated as solns. for intra-articular injection.
ADVANTAGE - The compsns. inhibit adhesion of inflammatory synovial membrane cells to joint cartilage tissue, alleviate inflammation of the synovial membrane, and have no toxicity or side effects.
Dwg.1/5
FS CPI
FA AB; DCN
MC CPI: B04-C02V; **B14-C06**
ABEQ US 5470578 A UPAB: 19960115
A method of treating **rheumatism** which comprises administering to mammals suffering from **rheumatism** a composition comprising between 0.1 to 80% lipid-bound glycosaminoglycan (gag) or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier, wherein said composition is administered in a dose of 0.1 to 2,000 mg/adult once a day or within several weeks.
Dwg.0/3

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=> d his

     (FILE 'HOME' ENTERED AT 15:52:25 ON 21 JAN 2003)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 15:52:46 ON 21 JAN 2003
L1             2 S HYALURONIC ACID/CN OR 9067-32-7
L2           753 S ?HYALURON?/CNS NOT L1
L3           435 S L2 NOT SQL/FA
L4           318 S L2 NOT L3
                 E CYCLOOXYGENASE/CN
L5             1 S E8
L6             2 S E3,E7
                 E MATRIX METALLOPROTEASE/CN
L7            15 S E3,E5-E13,E15-E17,E23,E24
L8             5 S E25,E36,E43,E45,E46
L9             4 S E50,E51,E55,E58
L10            1 S E61
L11            5 S E72,E75,E79-E81
L12            4 S E85,E89-E91
L13         1365 S (?METALLOPROTEINASE? OR ?METALLOPROTEASE?)/CNS
L14              STR
L15           31 S L14 CSS
L16         2264 S L14 FUL
                 SAV TEMP L16 FONDA700/A
L17          629 S L14 CSS FUL SUB=L16
                 SAV L17 FONDA700A/A

     FILE 'HCAPLUS' ENTERED AT 16:16:23 ON 21 JAN 2003
L18        10031 S L1
L19         3440 S L3
L20          151 S L4
L21        14614 S HYALURONIC ACID OR HYALURONATE OR HYALURONAN
L22        20161 S ?HYALURON?
L23        20696 S L18-L22
L24         1922 S L5
L25         9113 S L6
L26        13384 S (COX OR CYCLOOXYGENASE OR CYCLO OXYGENASE)(L)2 OR COX2
L27           13 S PROSTAGLANDIN(L)(ENDOPEROXIDASE OR ENDO PEROXIDASE)(L)(SYNTHA
L28           41 S L23 AND L24-L27
L29        26594 S L7-L13
L30          476 S L23 AND L29
L31          309 S L17
L32            4 S L23 AND L31

     FILE 'REGISTRY' ENTERED AT 16:21:16 ON 21 JAN 2003
L33         1635 S L16 NOT L17

     FILE 'HCAPLUS' ENTERED AT 16:21:22 ON 21 JAN 2003
L34            3 S L33 AND L23
L35           45 S L28,L32,L34
                 E ANTIRHEUMAT/CT
                 E E5+ALL
L36         4437 S E5,E4+NT
L37           48 S L23 AND L36
L38           91 S L35,L37
L39           77 S L23 AND (ANTIRHEUMAT? OR ANTI RHEUMAT?)
L40          136 S L38,L39
L41            6 S L40 AND ?CONJUGAT?
                 E TAMURA T/AU
L42          596 S E3-E5
                 E TAMURA TATSUYA/AU
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L43           57 S E3
                 E OKAMACHI A/AU
L44           15 S E3,E4
                 E CHUGAI/PA,CS
L45         3920 S E1-E4
                 E SEIYAKU/PA,CS
L46        15106 S E1-E6
                 E KABUSHIKI/PA,CS
L47            1 S E10E4
                 E KAISHA/PA,CS
L48        14062 S E2-E4
                 E KABUSHIKI/PA,CS
L49         8315 S E1-E4
L50            3 S L40 AND L42-L49
                 E WO99-JP2600/AP,PRN
L51            1 S E3,E4
                 E JP98-138329/AP,PRN
L52            1 S E4
                 E JP98-224187/AP,PRN
L53            1 S E4
                 E JP99-43064/AP,PRN
L54            1 S E4
L55            0 S L40 AND L51-L54
L56            1 S L51-L54 AND L42-L49

     FILE 'REGISTRY' ENTERED AT 16:28:57 ON 21 JAN 2003
L57            1 S 9001-92-7

     FILE 'HCAPLUS' ENTERED AT 16:29:06 ON 21 JAN 2003
L58        34671 S L57
L59       135094 S ?PROTEASE? OR ?PROTEINASE?
L60          972 S L23 AND L58,L59
L61            8 S L60 AND L42-L49
                 SEL DN AN 1-3
L62            3 S L61 AND E1-E9
L63            4 S L50,L56,L62 AND L18-L32,L34-L56,L58-L62
L64          117 S L23 AND L59 (L) ?MATRIX? (L) ?METALLO?
L65          246 S L40,L64
L66            4 S L56,L63
                 E JOINT/CT
                 E E5+ALL
L67         1229 S E2
                 E JOINT/CT
L68         3685 S E7-E28
                 E E6+ALL
L69         8769 S E6,E5+NT
                 E E13+ALL
L70         2565 S E2
L71           25 S L65 AND L67-L70
                 E CARTILAGE/CT
L72           13 S L65 AND E4-E20
                 E E3+ALL
L73           38 S L65 AND E7+NT
                 E RHEUMATISM/CT
                 E E3+ALL
                 E E2+ALL
L74           48 S L65 AND E4,E5,E3+NT
L75           77 S L71-L74
L76          170 S L40,L75
L77         3545 S (L1 OR L3 OR L4)(L)(THU OR USES OR BUU OR BAC OR DMA OR PAC O
L78           45 S L76 AND L77
L79           43 S L78 NOT L66
L80           79 S L76 AND (1 OR 63)/SC,SX
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L81          76 S L80 NOT L66
L82          84 S L79,L81
L83          53 S L82 AND (?CONJUGAT? OR SYNERG? OR BIND? OR BOUND? OR REACT? O
L84          19 S L83 AND L29
L85          21 S L83 AND L58,L59
                SEL DN AN 8 18
L86           2 S E1-E6
L87          27 S L83 NOT L84,L85,L86,L66
                SEL DN AN 8 15 18
L88           3 S E7-E15
L89          31 S L82 NOT L83-L88
                SEL DN AN 11 12
L90           2 S E16-E21
L91          11 S L66,L86,L88,L90
L92       12795 S L18-L20
L93          25 S L92 AND L24,L25
L94         580 S L92 AND L29,L58
L95           3 S L92 AND L31
L96           3 S L92 AND L33
L97           3 S L95,L96
L98           1 S L97 AND L91
L99          11 S L91,L98
L100         35 S L94 AND L36,L67-70
L101         40 S L94 AND L76
L102         59 S L100,L101
L103         31 S L102 NOT L82-L91,L99
                SEL DN AN 12
L104          1 S L103 AND E22-E24
L105         12 S L99,L104 AND L18-L32,L34-L56,L58-104
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 17:11:11 ON 21 JAN 2003
L106         19 S E25-E43

     FILE 'HCAPLUS' ENTERED AT 17:11:28 ON 21 JAN 2003
                SEL RN L66

     FILE 'REGISTRY' ENTERED AT 17:12:01 ON 21 JAN 2003
L107         36 S E44-E79
L108         23 S L107 NOT L106
L109          1 S L108 AND C39H59N5O11

     FILE 'HCAPLUS' ENTERED AT 17:13:17 ON 21 JAN 2003
L110          1 S L109
L111         12 S L110,L105

     FILE 'REGISTRY' ENTERED AT 17:13:39 ON 21 JAN 2003

     FILE 'HCAPLUS' ENTERED AT 17:13:54 ON 21 JAN 2003

     FILE 'REGISTRY' ENTERED AT 17:14:09 ON 21 JAN 2003
L112         20 S L106,L109

     FILE 'EMBASE' ENTERED AT 17:14:37 ON 21 JAN 2003
L113       7430 S L1
L114      10527 S L3
L115          0 S L4
L116       9891 S L21
L117      13801 S L22
L118      13801 S L113-L117
                E ANTIRHEUMATIC AGENT/CT
L119        555 S E3+NT AND L118
L120          1 S E3(L)CB/CT AND L119
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L121          13 S L118(L)CB/CT AND L119
                 SEL DN AN 6 7 9 10 12 13
L122           6 S L121 AND E1-E12
L123           7 S L120,L122
                 E CYCLOOXYGENASE/CT
L124        5725 S E46+NT
L125          62 S L118 AND L124
L126           1 S L124(L)CB/CT AND L125
L127           0 S L118(L)CB/CT AND L125
L128           8 S L123,L126
                 E MATRIX METALLOPROTEASE/CN
L129           0 S E4 AND L118
                 E METALLOPROTEASE/CN
                 E METALLOPROTIENASE/CT
                 E MATRIX METALLOPROTEASE/CT
L130          62 S E71+NT AND L118
L131           0 S E71(L)CB/CT AND L130
L132           0 S L118(L)CB/CT AND L130
L133           8 S L128 AND L113-L132

     FILE 'EMBASE' ENTERED AT 17:23:24 ON 21 JAN 2003
                 E ANTIRHEUMATIC AGENT+ALL/CT
                 E ANTIRHEUMATIC AGENT+ALL/CT

     FILE 'WPIX' ENTERED AT 17:24:16 ON 21 JAN 2003
                 E WO99-JP2600/AP,PRN
L134           1 S E3
                 E JP98-138329/AP,PRN
L135           1 S E4
                 E JP98-224187/AP,PRN
L136           1 S E4
                 E JP99-43064/AP,PRN
L137           1 S E4
L138           1 S L134-L137
                 E R03231+ALL/DCN
L139        1127 S E1
                 E R06437+ALL/DCN
L140         640 S E1
L141        1297 S C08B037-08/IC,ICM,ICS
L142        2330 S L21
L143        2427 S L21/BIX
L144        2832 S L22/BIX
L145        4071 S L139-L144
                 E OKAMACHI A/AU
L146           6 S E3
                 E TAMURA T/AU
L147         604 S E3-E7
L148           3 S L146,L147 AND L145
L149           3 S L138,L148
L150         134 S A61K031-728/IC,ICM,ICS
L151        4085 S L145,L150
L152           3 S L146,L147 AND L151
L153           3 S L149,L152
L154          26 S L151 AND ?MATRIX?(L)(?PROTEASE? OR ?PROTEINASE?)(L)?METALLO?
L155          18 S L154 AND INHIBIT?
L156          22 S L151 AND (?METALLOPROTEASE? OR ?METALLOPROTEINASE?)(L)INHIBIT
L157          24 S L155,L156
                 SEL DN AN 6 11 17 19 21 23 24
L158           7 S L157 AND E1-E17
L159           9 S L153,L158
L160          12 S L151 AND L26,L27
L161         117 S L151 AND ?RHEUMAT?
L162          26 S L151 AND (B12-D09 OR C12-D09 OR B14-C06 OR C14-C06)/MC
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L163          21 S L161 AND L162
L164          26 S L162,L163
L165          12 S L164 AND M782/M0,M1,M2,M3,M4,M5,M6
L166          14 S L164 NOT L165
                 SEL DN AN 1 7 9 12
L167           4 S L166 AND E18-E25
L168          11 S L159,L167 AND L134-L167
                 SEL DN AN 1-3 8 9 10
L169           6 S L168 AND E26-E39

     FILE 'WPIX' ENTERED AT 17:47:25 ON 21 JAN 2003
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